

NEURAL CORRELATES OF MINDFULNESS

Investigating self-related processes in mindfulness
meditators using functional magnetic resonance
imaging

Thesis (cumulative thesis)

Presented to the Faculty of Arts and Social Sciences
of the University of Zurich

for the degree of
Doctor of Philosophy

by
JACQUELINE LUTZ
of Zurich, Switzerland

Accepted in the Autumn Term 2015
on the Recommendation of the Doctoral Committee:

Prof. Dr. Lutz Jäncke (main advisor)

Prof. Dr. Uwe Herwig

Prof. Dr. Boris Quednow

Zurich, 2016

*“All of man’s difficulties
are caused by his inability
to sit, quietly, in a room
by himself.”*

Blaise Pascal, 1623-1662

*“I was going to change my shirt,
but I changed my mind instead.”*

Winnie the Pooh
(Alan Alexander, 1882-1956)

Acknowledgments

I would like to express my sincere gratitude to the many people who inspired and supported me and this work.

Prof. Lutz Jäncke for supervising this thesis. His broad neuroscientific knowledge and inspiring viewpoints were of great value on my academic journey. Prof. Uwe Herwig, for the opportunity to work in his neuroimaging group and the chance to follow my scientific interests while also gaining invaluable clinical experience. Prof. Boris Quednow, for his support and acceptance to co-examine this dissertation.

My co-workers, Prof. Annette Brühl and Hanne Scheerer, for fruitful discussions during all stages of this thesis. Andrea Weibel and the neuroimaging group for generously assisting me during data acquisition. Philipp Stämpfli, for his support and MR expertise.

I would like to thank Prof. Richard Davidson and his team for the opportunity to stay at the Center for Investigating Healthy Minds at the University of Madison, Wisconsin during my studies. It was an invaluable research and learning experience, for which I am deeply grateful.

A special thank you to all participants, meditators, and to Samuel Theiler and other meditation teachers who supported me finding participants – this thesis wouldn't have been possible without their help.

Thanks to my fellow doctoral students and all my dear friends and family for their emotional support during this time – and for the one or other mindless conversation to balance things out!

Last, but not least, I am grateful for my mother's enduring support and optimism.

Wim, thank you for everything! Celebrating this thesis and all the fortune we had together means a lot to me.

Contents

Acknowledgments	iii
Abbreviations	vii
Summary	ix
Zusammenfassung	xi
1 Introduction	1
2 Theoretical background	3
2.1 Mindfulness	3
2.1.1 Concept	3
2.1.2 Mindfulness research	4
2.2 Mechanisms of change in meditators	5
2.2.1 Self-related functions and the brain	5
2.2.2 Self-related functions and mental health	6
2.2.3 Mindful perspectives on self-related functions	7
2.2.4 Emotion regulation	9
3 Methods	11
3.1 Study samples	11
3.2 Experimental designs	12
3.3 Functional magnetic imaging	12
3.4 Analysing fMRI data	13
3.5 Trait mindfulness questionnaire	13
4 Aims and research questions	15
5 Empirical studies	17
Study 1: Neural correlates of mindful self-awareness in mindfulness medi- tators and meditation-naïve subjects revisited	18
Study 2: Altered processing of self-related emotional stimuli in mindfulness meditators	35

6	Discussion	57
6.1	Main findings	57
6.2	Integration	58
6.3	Limitations	61
6.4	Outlook	61
6.5	Conclusion	63
Appendix A Sample characteristics		80
Appendix B Supplementary material study 1		86
Appendix C Supplementary material study 2		89
Curriculum Vitae		93

Abbreviations

B	Baseline
BA	Brodman area
CMS	Cortical mid-line structures
DLPFC	Dorso-lateral prefrontal cortex
DMN	Default mode network
DMPFC	Dorso-medial prefrontal cortex
DMN	Default mode network
BOLD	Blood oxygen level dependent signal
EMO	Self-related emotional conditions
FEEL	Mindful self-awareness (body and emotions)
fMRI	Functional magnetic resonance imaging
FWE	Family-wise error correction
FFMQ	Five Facets Mindfulness Questionnaire
FSL	Software for the analysis brain imaging data
GLM	General linear model
LTM	Mid-to-long-term meditators
MBSR	Mindfulness-based stress reduction
MBCT	Mindfulness-based cognitive therapy
MNP	Meditation-naïve participants
MPFC	Medial prefrontal cortex
MWT-B	Mehrfachwahl-Wortschatz-Intelligenz-Test
NNSC	Negative not self-critical
NT	Neutral
OM	Open monitoring meditation
PANAS	Positive and Negative Affect Schedule
PCC	Posterior cingulate cortex
PFC	Prefrontal cortex
pre-SMA	Anterior portion of the supplementary motor area

R	Software environment for statistical analysis and graphics
ROI	Region of interest
SC	Self-criticism
SCS	Self-Compassion Scale
SDS	Zung Self-rating Depression Scale
SP	Self-praise
TAS	Toronto Alexithymia Scale
THINK	Cognitive self-reference (thinking about the self)
PPI	Psycho-physiological interaction
VMPCF	Ventro-medial prefrontal cortex

Summary

Mindfulness – a non-judgmental focus on present-moment experiences – is increasingly integrated into western therapy programs to alleviate mental health related problems (Kabat-Zinn, 2003). Mindfulness can be trained through meditation, and is thought to involve changes in self-related functions such as increased body awareness and decreased attachment to the self (Hölzel et al., 2011). In other words, mindfulness meditators practice “experiencing the self” instead of engaging in thoughts and judgements about the self. This is hypothesized to reduce problems associated with an exacerbated self-focus and brooding on negative aspects of the self, while increasing emotional balance, for example in the face of self-criticism (Vago and Silbersweig, 2012). Despite the clinical relevance of such changes, neuroscientific investigations of self-related processes in mindfulness meditators are scarce (Tang et al., 2015), particularly regarding their neural correlates. This thesis describes two experiments on self-related functions and emotions during functional magnetic imaging (fMRI). In both experiments, the subjects consisted of 22 experienced, regular mindfulness meditators (LTM) and 22 meditation-naïve participants (MNP).

The first study compared mindful awareness of body and emotions (“experiencing the self”) to cognitive self-reference (“thinking about the self”). Mindful awareness has been associated with activations in somatosensory brain regions and reduced activations in cortical mid-line structures in novice meditators (Farb et al., 2013), and partly in untrained individuals (Herwig et al., 2010). Here we investigated this contrast in regular mindfulness meditators and compared them to untrained individuals.

During mindful self-awareness we found increased activation in somatosensory areas in both groups, consistent with Herwig et al. (2010). Decreases in regions associated with cognitive self-reference were also found in both groups, however they were larger in LTM. Interestingly, neural activations during mindful awareness indicated that LTM engaged less in verbalizing their experience compared to MNP. Overall, these results corroborate the link between meditation training and neural correlates of mindful self-awareness (Farb et al., 2013). However, group differences were less pronounced than previously suggested, indicating that states of mindful awareness are accessible to untrained individuals.

The second study employed individually tailored stimuli of self-praise and self-criticism to investigate self-related emotion processing in meditators. Activations in emotion-generative structures (such as the amygdala) and emotion-regulative structures in the prefrontal cortex have been found during self-criticism (Doerig et al., 2014). We hypothesised to see group differences in these regions and in affective ratings after self-appraisals.

When comparing affective ratings after self-criticism and self-praise, LTM showed a smaller difference between these conditions than MNP. On the neural level, however, the group comparison revealed that LTM had stronger activations in emotion-generative regions during self-appraisals, indicating higher emotional reactivity (Taylor et al., 2011). LTM further displayed stronger activations in the dorso-medial prefrontal cortex (DMPFC). The DMPFC activation correlated with a non-reacting attitude towards inner experience, as assessed in a trait mindfulness questionnaire. This could reflect that meditators face self-appraisals in an accepting and non-reactive way (Hölzel et al., 2007). Further, the DMPFC activation in LTM showed no difference in functional connectivity to other regions during self-appraisals compared to neutral stimuli, while in MNP increased connectivity between DMPFC and posterior mid-line and parietal regions was found. Thus, meditators might have processed self-related emotions with less self-focused attention than MNP (Garrison et al., 2014).

In summary, cortical prefrontal mid-line structures were less active in meditators during mindful self-awareness, while a partly overlapping DMPFC region was stronger activated during self-criticism and self-praise. The cross-sectional design of our studies limits direct causal conclusions, but the results point towards meditation-training related improvements in present-moment awareness, and a more accepting attitude when facing self-appraisals.

Zusammenfassung

Achtsamkeit wird in vielen, vor allem östlichen Traditionen beschrieben, und bezeichnet eine nicht-wertende Aufmerksamkeit auf Erfahrungen im Moment, z.B. Körperempfindungen, Gedanken und Gefühle (Kabat-Zinn, 2003). Eine achtsame Haltung kann unter anderem mittels Meditation geübt werden. Achtsamkeitstraining wird auch vermehrt in der Psychotherapie eingesetzt. Positive Effekte von Achtsamkeit gehen wahrscheinlich mit Veränderungen in selbst-bezogenen Prozessen einher (Hölzel et al., 2011). Meditierende üben zum Beispiel, sich selbst im Moment wahrzunehmen, ohne sich in Gedanken und Urteilen zu diesem Selbst zu verlieren. Dies kann negativen selbstbezogenen Prozessen entgegenwirken, wie zum Beispiel einem zu starken Fokus auf das Selbst, dem Grübeln über negative Aspekte des Selbst und übertrieben starken selbstbezogenen Emotionen (z.B. starke Selbstkritik) (Vago and Silbersweig, 2012).

Trotz der klinischen Relevanz solcher Vorgänge, z.B. im Bezug auf die Depressionsbehandlung, gibt es bisher nur wenige Studien, die Veränderungen in selbst-bezogenen Prozessen in Achtsamkeits-Meditierenden zu erfassen versuchen. Die vorliegende Dissertation untersucht selbstbezogene Prozesse und ihre neuronalen Korrelate, mittels funktioneller Magnetresonanz Bildgebung (fMRI), in 22 erfahrenen Achtsamkeits-Meditierenden (LTM) und vergleicht sie mit einer Gruppe Meditations-Unerfahrener (MNP).

In der ersten Studie untersuchten wir, in welchem Ausmass die achtsame Wahrnehmung von Körper und Gefühlen (“Fühlen”) im Vergleich zum Nachdenken über sich selbst (“Denken”) zu vermehrter Aktivierung in sensorischen Körperwahrnehmungs-Arealen und reduzierter Aktivierung in gedanklich, selbst-bezogenen Mittellinien-Arealen führt. Diese Muster zeigten sich nach kurzem Achtsamkeitstraining (Farb et al., 2013), und zum Teil bereits in Meditations-Unerfahrenen (Herwig et al., 2010). Jedoch hat noch keine Studie diese Befunde in erfahrenen Meditierenden überprüft.

In unserer Studie führte “Fühlen” zu Aktivierungen in Körperwahrnehmungs-Arealen in beiden Gruppen. Reduzierte Aktivierung in frontalen Mittellinien-Strukturen waren hingegen ausgeprägter in LTM, was darauf hinweist, dass diese Gruppe weniger selbstbezogene Bewertungen während “Fühlen” machte. Ausserdem deuteten reduzierte Aktivierungen in sprachbezogenen Arealen darauf hin,

dass LTM ihre Erfahrungen während “Fühlen” weniger stark verbalisierten. Die Ergebnisse legen Fortschritte in achtsamer Wahrnehmung aufgrund von Achtsamkeitstraining nahe. Jedoch zeigten auch MNP einige dieser Aktivierungen. Es scheint also, dass kurze Phasen achtsamer Wahrnehmung auch für Untrainierte zugänglich sind.

In der zweiten Studie untersuchten wir die Verarbeitung von Selbstkritik und Selbstlob. Meditierende trainieren eine akzeptierende Haltung gegenüber Emotionen. Deshalb erwarteten wir Unterschiede in Emotionsgenerierenden Strukturen (z.B. der Amygdala) aber auch in präfrontalen, Emotionsregulierenden Strukturen. Ausserdem erfragten wir die Stimmung nach Selbstlob und Selbstkritik.

Meditierende berichteten weniger emotionale Auslenkung nach Selbstlob und Selbstkritik. Auf der neuronalen Ebene hingegen, zeigten Meditierende stärkere Aktivierungen in Emotionsgenerierenden Strukturen, vor allem während Selbstlob. Dies deutet auf stärkeres emotionales Erleben in dieser Gruppe hin. Wir fanden ausserdem stärkere Aktivierungen im dorso-medialen präfrontalen Kortex (DMPFC). Diese Aktivierung korrelierte mit einer nicht-reagierenden Haltung gegenüber Erfahrungen (eine Facette des erhobenen Achtsamkeits-Fragebogens) und könnte eine akzeptierende Haltung gegenüber Selbstlob und Selbstkritik bedeuten. Eine funktionelle Konnektivitäts-Analyse während selbstbezogener Emotionsprozesse zeigte, dass in MNP die DMPFC-Aktivierung stärker mit Aktivierungen in anderen Mittellinien- und parietalen Strukturen verbunden war. Dieselbe Analyse zeigte keine Unterschiede in der funktionellen Konnektivität in LTM. Dies könnte bedeuten, dass Meditierende die selbstkritischen und selbstlobenden Adjektive mit weniger selbstbezogener Aufmerksamkeit verarbeiteten als Meditations-Unerfahrene (Garrison et al., 2014).

Zusammenfassend fanden wir reduzierte Aktivierungen in präfrontalen Mittellinien-Strukturen in Meditierenden während achtsamer Selbstwahrnehmung. Hingegen fanden wir in einer teilweise überlappenden DMPFC Region verstärkte Aktivierung während Selbstkritik und Selbstlob. Diese Resultate widerspiegeln wahrscheinlich eine “erfolgreichere” achtsame Wahrnehmung von Körper und Gefühlen im Moment, und eine akzeptierende Verarbeitung selbstbezogener Emotionen.

Trotz der Einschränkung solcher Querschnittsstudien im Bezug auf kausale Rückschlüsse, geben die hier vorgestellten Studien weitere Hinweise auf Veränderungen in selbstbezogenen Prozessen im Zusammenhang mit Meditationstraining.

Chapter 1

Introduction

Eastern meditation and mindfulness techniques have found their way from monasteries into western mainstream. Particularly the last 30 years have seen a rising interest in these techniques, mainly driven from western clinical psychology. Mindfulness promotes a non-judgmental focus on present-moment experience, and has been associated with improved mental health and well being, by alleviating stress and fostering emotional balance. With these promises in mind, numerous mindfulness-based clinical programs have been developed.

Roughly in the same period, functional magnetic resonance imaging (fMRI) has allowed an unprecedented view into human brain activity. Research into the effects of mindfulness training thus increasingly investigated neural underpinnings of associated behavioral changes. Based on these results, several integrative theoretical frameworks have been established to explain the salutary effects of mindfulness. Most of these propose mechanisms of change associated with changes in self-related processes and emotion regulation, such as less attachment and a non-judgmental attitude towards the self, and increased present-moment awareness. But the exact mechanisms are still poorly understood, particularly on the neural level, and literature on this topic is still sparse.

This thesis aims to advance our understanding of mindfulness-related changes in self-related processes. It is built around two studies on self-reference, body awareness and self-related emotions in experienced mindfulness meditators, and is structured as follows: Chapter 2 lays the theoretical ground, by defining mindfulness and introducing self-related processes and emotion regulation. The concepts are integrated on a theoretical level and regarding their neural correlates. Further, previous findings on changes in self-referential processes related to mindfulness are discussed. The methods chapter (3) describes the samples and methods employed in the studies conducted as part of this thesis. Chapter 4 states the aims of the two studies. The studies and results follow in the empirical chapter (5). Chapter 6 concludes the thesis with a summary of the results, an integration into the theoretical framework, and a discussion of limitations and future directions.

Chapter 2

Theoretical background

This chapter introduces the concept of mindfulness, how it is related to meditation and how it can be studied. Further, meditation-related neurobiological changes regarding the self and emotion regulation are discussed. These changes are explored in the light of current research – particularly in the field of neuroscience – and discussed regarding their clinical relevance.

2.1 Mindfulness

2.1.1 Concept

The Eastern roots of mindfulness date back about 2500 years to the term *Sati* in the ancient Indian language Pali (Pali Text Society, 1921). It describes the faculty of a *present mind*, which can be cultivated by means of meditation training (Silananda and Heinze, 1995). Several forms of meditation exist to cultivate mindfulness, including *open monitoring* (OM) techniques (Lutz et al., 2008), which involve nonreactive monitoring of body states and the contents of the mind itself. Meditation ultimately has the goal of reducing suffering (Mikulas, 2007; Silananda and Heinze, 1995), an interest, which is shared by western psychology.

Increasingly, mindfulness techniques have been integrated into modern psychotherapeutic programs (Baer, 2003). John Kabat-Zinn, founder of the first mindfulness-based interventions, such as mindfulness-based stress reduction (MBSR), coined the mindfulness definition “paying attention in a particular way: on purpose, in the present-moment, and non-judgmentally” (Kabat-Zinn, 1994). Bishop et al. (2004) propose a similar definition, consisting of the two components *attention to momentary experiences* and an *accepting attitude* towards these experiences. However, there is disagreement whether mindfulness in its western adaptations reflects all important aspects originally indicated by *Sati* (Chiesa, 2012; Christopher et al., 2009; Grossman and Van Dam, 2011; Shapiro et al., 2006). Moreover, mindfulness has been introduced as a psychological construct independent of Eastern influences

(Langer and Moldoveanu, 2000). Further complexity for defining mindfulness stems from the fact that it can simultaneously be used to describe a particular *state* of mind, a *trait*, reflecting a persons natural tendency to be mindful in everyday life, or a *meditation technique* (Davidson, 2010; Vago and Silbersweig, 2012). In short, definitions of mindfulness remain controversial both among Buddhist scholars and mindfulness researchers (Hart et al., 2013).

Despite the lack of a unified definition, mindfulness has been associated with a wide range of positive effects on mental health, such as lower levels of stress, and psychopathological symptoms, better self-regulation, emotional balance and general well-being, both in healthy individuals and clinical populations (Baer, 2003; Hart et al., 2013; Keng et al., 2011). The size of these effects varies across meta-studies. Some find that effects might not be superior to other active treatments (Goyal et al., 2014; Khoury et al., 2013) and specific causal links between mindfulness and these effects have rarely been established so far (Chiesa and Serretti, 2010; Eberth and Sedlmeier, 2012; Gu et al., 2015). The current state of mindfulness research partly reflects the still relatively young research field and the multi-faceted nature of mindfulness.

2.1.2 Mindfulness research

Mindfulness as a state has mainly been explored in meditators during meditation (for an overview see Cahn and Polich, 2006), but some studies have also looked into short phases of mindful states in meditation-naïve subjects (Herwig et al., 2010; Lutz et al., 2014; Farb et al., 2007).

At the same time, mindfulness training increases trait mindfulness (Kiken et al., 2015). Thus, beyond improving mental capabilities for meditation, mindfulness training is assumed to influence mental functions in everyday life. In the language of neuroscience, the repeated mental activity of meditation is believed to cause enduring structural and functional changes in the brain (Davidson and Lutz, 2008; Luders et al., 2009; Fox et al., 2014), similar to other, well-documented accounts of practice induced plasticity (Bezzola et al., 2012; Jäncke, 2013). To study such changes, longitudinal and cross-sectional strategies are employed. Longitudinal studies measure the same participants of mindfulness programs or meditation retreats over time, while cross-sectional studies compare experienced meditators with meditation-naïve participants at one time-point. Only longitudinal studies can reach causal statements about mindfulness-related changes (Davidson, 2010), but they require extensive resources. Furthermore, later stages of mindfulness training

are hard to capture with longitudinal studies, since it would require to follow meditators over long periods (Tang et al., 2015). Therefore, cross-sectional studies, despite lacking the prospect of causal conclusions, remain a valuable strategy to gain first evidence for changes related to mindfulness training or for studying later stages of mindfulness training.

2.2 Mechanisms of change in meditators

Related to the multifaceted nature of mindfulness, different mechanisms of change have been proposed. A widely referred theoretical framework by Hölzel et al. (2011) describes a set of interrelated components of enhanced self-regulation along with their neurobiological correlates. These are: *increased attention* and *body awareness*, *better emotion regulation* and a *change in the perspective on the self* (see Figure 2.1). A newer description by Tang et al. (2015) subsumes the self-related functions (body awareness and perspective on the self). Another neurobiologically informed model even describes mechanisms of change purely from the perspective of changes in self-related functions (Vago and Silbersweig, 2012). But what are self-related functions, and how does mindfulness training relate to them?

2.2.1 Self-related functions and the brain

The self has fascinated mankind throughout its history. Philosophers and psychologists discussed its nature and described different forms of self-functions (Damasio, 2000; James, 1890; Neisser, 1988). Most theories distinguish between some form of body-centered, “minimal” self and cognitive, conceptual self-defining functions. In simple words, the former relates to experiencing our self in the present moment, while the latter subsumes the concepts and thoughts we have about this self. These two aspects have also been studied with neuroscientific methods (Gallagher, 2000). In this thesis, the term *experiential self* will be employed for the former and *cognitive self* for the latter. Self-reference describes processes related to the cognitive self, while self-related functions subsume all processes related to the self.

On the neuro-anatomical level, the experiential self has been associated with areas related to sensory processing and body awareness, such as the insula and somatosensory cortex (Bauer et al., 2014; Craig, 2003; Critchley et al., 2004), and multisensory integration regions, like the temporo-parietal junction (TPJ). The TPJ has been associated with consciousness, embodiment and agency (Blanke and Mohr, 2005; Ionta et al., 2014).

Neural regions associated with the cognitive self have mostly been identified in fMRI studies, which utilize stimuli, such as trait adjectives, and let participants judge, whether the stimulus describes themselves, versus someone else (Northoff et al., 2006). Another approach is to present participants with previously chosen, self-describing stimuli (Doerig et al., 2014). Some studies use no external stimuli, but instruct participants to initiate specific self-related processes, like thinking about the self (Brühl et al., 2014; Herwig et al., 2010). Results of these studies relate the cognitive self to cortical mid-line structures (CMS), including the dorso-medial prefrontal cortex (DMPFC), ventro-medial prefrontal cortex (VMPFC), posterior cingulum (PCC) and precuneus (Farb et al., 2007; Herwig et al., 2010; Northoff and Bermpohl, 2004). Posterior parts of the CMS have been linked to autobiographical memory, the DMPFC to judgement about the self, and the VMPFC and other rostro-medial prefrontal regions to affective self-reference (Schmitz and Johnson, 2006). Together, these CMS structures have been suggested to constitute the core of our conscious, cognitive self (Northoff et al., 2006).

Another line of research studies the brain “at rest”, i.e. when participants are not conducting a specific task. A set of regions, which display coherent neural activations during such a resting state, have been described as the default mode network (DMN) of the brain (Gusnard et al., 2001; Raichle et al., 2001). Interestingly, these regions strongly overlap with the activations observed in self-referential tasks (Whitfield-Gabrieli et al., 2011), indicating that self-reflection might constitute a “psychological baseline” (Northoff et al., 2006) of the brain in absence of a task. However, the exact nature and implication of the DMN is still debated (Callard and Margulies, 2014).

In summary, self-related regions in the brain are commonly described as structures subserving body awareness and interoception, such as the insula, somatosensory cortex, and TPJ, and structures involved in higher order, cognitive self-reference, such as frontal and parietal CMS.

2.2.2 Self-related functions and mental health

Disfunctional self-referential processes have been associated with various mental disorders. Depression, for example, is characterized by a stronger self-focus and self-criticism (Greenberg and Pyszczynski, 1986; Joormann and Gotlib, 2010; Mor and Winquist, 2002; Northoff, 2007) and increased rumination about negative aspects of the self (i.e. brooding) (Disner et al., 2011; Hamilton et al., 2011; Nolen-Hoeksema et al., 2008). On the neural level, research suggests that such symptoms are at least partly reflected in functional changes in the CMS. During self-referential tasks,

2.2. MECHANISMS OF CHANGE IN MEDITATORS

depressed patients showed increased activation in the VMPFC (Lemogne et al., 2012; Northoff, 2007). Similarly, during resting state, depression was associated with hyper-activation and hyper-connectivity in the DMN (for an overview see Whitfield-Gabrieli and Ford, 2012).

2.2.3 Mindful perspectives on self-related functions

Mindfulness training might influence self-related functions through increased body awareness and a changed perspective on the nature of the self.

Focused attention on body sensations, such as the breath, is part of many meditation techniques, including OM. Attention on body sensations is believed to increase body awareness in meditators. Structural changes in the insula and other sensory cortices in meditators might reflect this mechanism (Fox et al., 2014). However, direct behavioral evidence for increased body awareness in meditators, for example as assessed in classical heart-beat detection tasks, is still scarce (Khalsa et al., 2008). Two recent studies found evidence for increased body awareness in the form of better tactile-discrimination (Fox et al., 2012) or more accurate detection of physiological changes related to emotions (Sze et al., 2010).

Awareness of the body can be seen as the opposite of rumination. Body sensations always take place in the present moment, thus they can act as an anchor to (re-)direct the attention to the present moment. In this way, meditation might impede an exaggerated cognitive self-focus or being caught up in thoughts about the past or future (Brewer et al., 2011), which has been associated with negative mood (Killingsworth and Gilbert, 2010).

Direct neuroscientific research on mindful self-awareness and self-reference in meditators is scarce. An often-cited study by Farb et al. (2007) compared participants after an MBSR course to subjects without mindfulness training. Both groups performed experiential self-awareness compared to cognitive self-reference vis-a-vis general trait adjective stimuli. The study found increased activations in MBSR participants in regions associated with body awareness (insula, somatosensory cortex), while activations in CMS regions and the amygdala were reduced. This is in line with the illustrated polarity between present-moment awareness and cognitive self-reference. The reduced amygdala activation even indicates reduced emotional arousal during experiential self-awareness in meditation trained subjects. However, an experiment on mindful awareness in a sample of meditation-naïve participants, which used no stimuli, also reported decreased CMS and amygdala, and increased insular and somatosensory activations (Herwig et al., 2010). Thus, a state of mindful awareness might already induce a shift away from habitual

self-reference in untrained individuals.

Another way in which mindfulness might promote healthy self-related processes, is related to the Buddhist view of the self as a transient entity (Fulton, 2010). Particularly during OM meditation, meditators observe the contents of the mind itself. The arising thoughts and feelings should be met in a non-judgmental and non-reactive way. Such an observer’s view – sometimes called meta-awareness – weakens the identification of the observer with her thoughts and feelings, and challenges the concept of a static self over time. This change in the perspective of the self should reduce identification and attachment to the self. Brown et al. (2007) speak of a “quieting of self-concept”. This mechanism seems harder to grasp and most likely requires extensive mindfulness training. At the same time it has several interesting implications for mental health.

On the one hand, it could reduce the aforementioned symptoms associated with a strong self-focus. On the other hand, if emotions and thoughts are perceived as simple mental phenomena, their relevance and emotional impact should be reduced (Fulton, 2010). Hence, emotional reactions towards self-related emotions such as self-criticism should be diminished (more in section 2.2.4). Such more profound changes in the perspective on the self have not been extensively studied in mindfulness research. Some qualitative and questionnaire studies report changes in the perspective on the self in meditators, resulting in higher self-acceptance and more self-esteem (Hölzel et al., 2011; Kerr et al., 2011). Neuroscientific accounts of such changes are scarce, but have found evidence for changes in mid-line regions (Hölzel et al., 2011). Studies on brain networks during meditation showed decreased DMN activations, and higher connectivity between the DMN and regions implied in cognitive control (Brewer et al., 2011). But these results might not reflect enduring changes in self-related processing beyond meditative states. Evidence for lasting changes of self-processing is provided by a classic resting state study in meditators, i.e. when meditators were not meditating (Jang et al., 2011), which found changes in the DMN similar to the ones described by Brewer et al. (2011). Thus, habitual self-processing might indeed change as a result of repeated mindfulness training. Finally, the reported decreases in DMN in Farb et al. (2007)’s study could be mentioned in this context. However, the study focused on aspects of body awareness rather than differences during cognitive self-reference. To our knowledge, no neuroscientific study looked at active cognitive self-reference in meditators. Thus, we have very limited knowledge of neural correlates of these processes in meditators (Hölzel et al., 2011; Tang et al., 2015).

In summary, there is some evidence that mindfulness training changes neural corre-

2.2. MECHANISMS OF CHANGE IN MEDITATORS

lates of self-related processes (Brewer et al., 2011; Hölzel et al., 2011; Tang et al., 2015), by increasing body awareness and present-moment focus, reducing cognitive self-reference and potentially weakening self-attachment. Some of these mechanisms are further closely related to emotion regulation, which will be discussed in the following section.

2.2.4 Emotion regulation

Similar to mindfulness, the interest in emotion regulation has risen, as lower emotional reactivity and better emotion regulation skills are related to mental health (Gross and Muñoz, 1995).

Emotions are triggered by personally relevant, internal or external stimuli. These stimuli attract an individual's attention and are appraised regarding their value and importance for the individual (Gross and Thompson, 2007). This emotion-generative process leads to an emotional response, like fear, anger or joy, and can be influenced consciously or unconsciously at different stages. Commonly described adaptive strategies to regulate emotions include attention-deployment, i.e. directing attention towards or away from an emotional stimulus, and reappraisal, i.e. re-interpreting the stimulus in a more neutral way (Ochsner et al., 2002; Ochsner and Gross, 2005). On the neural level, emotion regulation is ascribed to prefrontal regulatory structures (DMPFC, DLPFC), which exert a *top-down* influence on emotion-generative, *bottom-up* regions, encompassing the amygdala, hippocampus and striatum (Ochsner et al., 2002; Ochsner and Gross, 2005; Phillips et al., 2003). Mindfulness has been suggested to improve emotion regulation via attentional control, body awareness and more successful reappraisal. Directing attention on and verbal labeling of emotions (affect labeling) seems to already reduce amygdala activation (Lieberman et al., 2007) in meditation-naïve participants. And higher trait mindfulness was associated with increased top-down control during an affect labeling task, indicating greater emotion regulation skills in more mindful individuals (Creswell et al., 2007). Further, increased awareness of body sensations and emotions could help to become aware of emotions earlier in the emotion-generative process. Emotion regulation strategies could then be applied at an earlier stage and reduce affective responses more efficiently. The increases in attentional control in meditators (Brefczynski-Lewis et al., 2007), has further been related to general gains in cognitive functions like working memory (Chambers et al., 2007). Such gains might free prefrontal resources for applying emotion regulation strategies such as reappraisal more effectively (Davis and Hayes, 2011). Indeed, increased prefrontal top-down activity when reappraising emotional stimuli was documented

in subjects with higher trait mindfulness scores (Modinos et al., 2010).

However, regulating or changing emotions seems contrary to mindful attitudes of non-judgmental awareness, non-reactivity, and acceptance. In an attempt to reconcile the concepts, it has been suggested that meditators don't reappraise the emotions but the emotion-generative process itself, by observing it from a meta-cognitive perspective. Another interesting suggestion by Chiesa et al. (2013) and Zeidan (2015) places effects of short-term mindfulness practice closer to improvements in classic emotion regulation, reflected in increased top-down regulation of emotions (e.g. increased reappraisal). In contrast, later stages of mindfulness training might be characterized by reduced top-down regulation in the face of emotional stimuli (Taylor et al., 2011), reflecting the non-judgmental and accepting aspects of mindfulness.

Overall, better emotion regulation skills are probably related to increased attentional and cognitive resources and heightened body awareness in meditators. The accepting attitude towards experiences seems to contradict classical notions of emotion regulation, but might present an additional mechanism in which experienced meditators influence the emotion-generative process. Figure 2.1 summarizes the discussed mechanisms of change in meditators and their neural correlates.

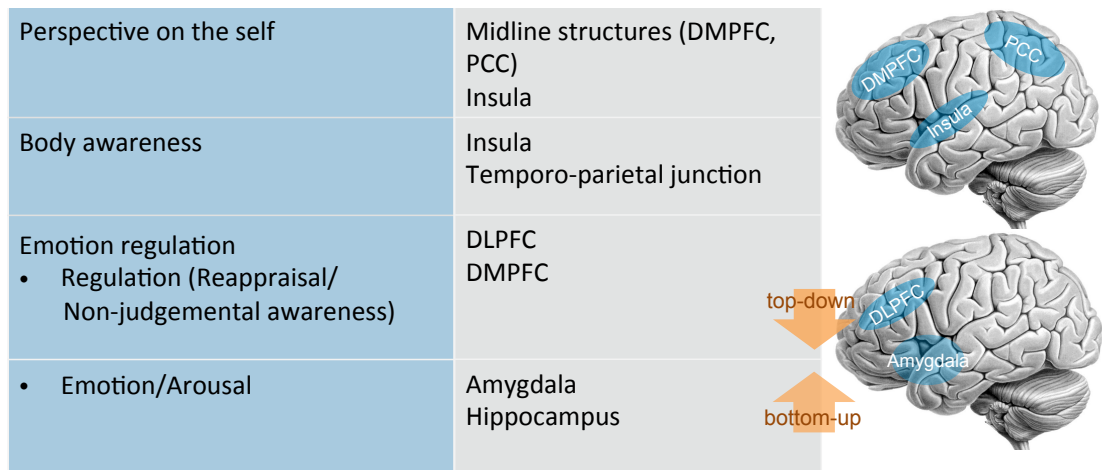


Figure 2.1: Neural correlates of mindfulness-related changes in self-related functions and emotion regulation. Adapted from Hölzel et al. (2011).

Chapter 3

Methods

This chapter introduces the study samples, experiments, methods and analyses techniques used in the two empirical studies.

3.1 Study samples

Vipassana meditation or related open monitoring (OM) techniques (Lutz et al., 2008) have particularly been linked to better emotion regulation and have greatly inspired secular, clinical programs (Chiesa and Malinowski, 2011). Marked changes in the perspective on the self and habitual emotion processing are likely to occur at later stages of meditation training (Hölzel et al., 2011). For these reasons, we recruited experienced mindfulness meditators, with OM experience (Lutz et al., 2008). Minimal inclusion criteria were: more than one year experience in meditation with a minimum of one year in the Vipassana tradition; a current meditation practice in an OM technique (at least one hour per week); and retreat experience in the Vipassana tradition.

The final sample consisted of 22 meditators with an average of 4862 lifetime practice hours in Vipassana (range: 281-18325), and an average of 5971 hours when counting total meditation experience (range: 506-18805). The current sample was therefore well above the level of introductory mindfulness courses. There is no standardized way to classify meditators regarding their experience. Following Zeidan (2015)'s classification, the sample consists of 16 adept meditators (<1000 hours), and six expert meditators (around or above 1000 hours). The sample is thus in the range of meditators studied in cross-sectional investigations, such as Hölzel et al. (2007) or Taylor et al. (2011). However, as opposed to cross-sectional studies by Brefczynski-Lewis et al. (2007), Lutz et al. (2009) and others, our sample did not include very high expertise levels >20000 hours.

Mindfulness meditators were matched with 22 meditation-naïve participants for age, gender, years of education, highest educational degree, general field of occupation, and crystalline intelligence.

Both experiments in this thesis were carried out on these two samples. The samples are characterized in more detail in chapter 5.

3.2 Experimental designs

Experiment 1 is based on an established paradigm by Herwig et al. (2010). Two different self-related processes were explored in a slow event-related design: a mindfulness-related awareness of body sensations and feelings in the present moment and cognitive self-reference (thinking about the self). In contrast to most studies on self-related functions, the paradigm refrains from using external stimuli, in order to resemble every-day self-related thoughts and perceptions and maximize ecological validity. Further, we believe this setup is easier to follow by mindfulness-untrained individuals, since the focus can remain purely on the self-related task.

Experiment 2 employed an innovative approach by Doerig et al. (2014) to study self-related emotions. The authors used participant’s previously chosen, and thus relevant, self-critical adjectives as stimuli. Here, the paradigm was extended to include self-praising words. This would allow inference on valence-overarching effects and offer first insights into positive self-appraisals in meditators.

Both experiments were extended with self-report affective ratings. This way, fMRI data could potentially be supplemented with phenomenological insights regarding subjective experience related to self-reference and self-related emotions. Moreover, it would allow to explore potential behavioral differences between the groups.

3.3 Functional magnetic imaging

Functional magnetic imaging (fMRI) is a widely used, non-invasive method in neuroscience to make inferences about brain activity (Logothetis, 2008). FMRI is based on detecting changes in relative levels of oxygenated and deoxygenated blood. The assumption is that active brain regions consume more energy, which triggers a hemodynamic response and increases oxygenated blood flow to that region. This relative increase in oxygenated blood can be detected by the MRI scanner, since the paramagnetic property of oxygenated blood increases the magnetic signal (Jäncke, 2013). The blood oxygenation level dependent (BOLD) signal is thus an indirect measure of brain activity. Although the exact relation between brain activation and the BOLD signal is still under investigation, evidence suggests that the signal corresponds to neural input and local processing in a region (Logothetis et al., 2001).

3.4 Analysing fMRI data

Statistical inferences on brain activation can be gained with a general linear model (GLM) approach. The observed time-series in a small brain volume (voxel) are predicted by task-regressors in a mass univariate approach, i.e. for each voxel separately. Regression weights can then be subjected to standard statistical tests (e.g. t-tests), to compare different conditions and groups. Results of these analyses are usually displayed in parametric maps, showing the fit between the experimental manipulation and the observed voxel activation. A higher fit between a specific brain region and a task regressor indicates that activity in a region was higher during this condition. Thus, such an approach provides insight into the functional specialization of a region.

Recently, the study of dynamic interactions between different regions has been gaining more interest (O'Reilly et al., 2012) and a number of methods have been developed to study them. Some measure effective connectivity, by assuming underlying connectivity models. They allow causal inferences about brain interactions, which is close to the intuitive notion of functional connections between regions (Friston, 1994). One method for measuring effective connectivity is the psychophysiological interaction analysis (PPI). It was introduced by Friston et al. (1997), and is well suited for task-based connectivity analysis, as it is based on the GLM approach (Poline and Brett, 2012). By adding the activation time-series from a region of interest in the brain (seed) to the GLM, a PPI regressor can be constructed to model the interaction between this seed and other regions in the brain depending on the task. In other words, the PPI identifies areas in the brain which are more strongly related to that seed during a specific task compared to another.

In this thesis, fMRI data are mainly analyzed by computing task- and group-contrasts to localize relevant brain areas. In study 2, an activation result is further explored in a PPI analysis, to study differences in functional connectivity between brain regions during self-appraisals compared to neutral words, and to explore differences in connectivity between groups.

3.5 Trait mindfulness questionnaire

The Five Facets Mindfulness Questionnaire (FFMQ, Baer et al., 2006), was developed based on five mindfulness questionnaires, using a factor analytic approach. It consists of 39 items, rated on a 5-point Likert-type scale, which describe five separable facets of mindfulness: 1) observing and, 2) describing experiences, 3)

acting with awareness, and applying a 4) non-judgmental and 5) non-reactive attitude towards inner experiences. The first three aspects relate mostly to aspects of attention and body awareness while factors four and five are related to emotion regulation in Hölzel et al. (2011)'s framework. The basic factor structure has been validated (Christopher et al., 2012), however, some limits regarding the comparability between meditators and non-meditators are discussed. The two studies presented in this thesis utilize the FFMQ as a self-report trait mindfulness measure, mainly for the possibility to examine group differences in light of specific aspects of mindfulness (Baer et al., 2006).

Chapter 4

Aims and research questions

The goal of the present work is to help answer the question: “Can states of mindfulness and mindfulness training influence the way an individual processes self-related information?”. As discussed in the previous chapters, the empirical basis in this area is sparse. It relies on few samples of meditators and is often limited to participants of introductory mindfulness courses. Thus, accounts of changes in self-related processes are largely based on mindfulness theory or self-report data. Nevertheless, mindfulness interventions have been integrated into many clinical programs partly because healthier self-related functions are assumed.

The present work attempts to expand our knowledge on changes in self-related processing associated with mindfulness on the neural level. During fMRI, different self-related processes, like awareness of body and feelings, self-referential thinking and processing of self-related emotional stimuli were investigated in the same sample of mid-to-long-term meditators (LTM) and meditation-naïve participants (MNP). In addition, behavioral data like facets of trait mindfulness, affective ratings during the tasks, and meditation experience were employed to further explore group differences.

In *study 1*, states of mindful awareness of body sensation and feelings (FEEL) were contrasted with thinking about the self (THINK).

Previous findings with this paradigm reported increased activations in somatosensory regions and left inferior-lateral prefrontal cortex and decreased activation in ventral prefrontal and posterior cortical mid-line structures (CMS) and the amygdala (Herwig et al., 2010), indicating increased focus on sensations and reduced cognitive self-reference according to the framework by Hölzel et al. (2011).

The primary goal of the present study was to investigate, in which of these areas mindfulness meditators would differ in a direct group comparison. Based on findings by Farb et al. (2007), greater decreases in CMS, left prefrontal and amygdalar regions were expected in LTM during FEEL compared to THINK.

A second goal was to address contradictory results regarding mindfulness-related brain activations in meditation-naïve participants during mindful awareness. Herwig

et al. (2010) reported increased somatosensory activations and reduced amygdala and prefrontal CMS areas in mindfulness-naïve, while Farb et al. (2007) mainly reported such findings for meditators. The experimental setup in Herwig et al. (2010) and the current study employed no external stimuli presumably facilitating meditation-naïve participants to enter a mindful state. Thus, some of the discussed mindfulness-related activations and deactivation were hypothesized also in MNP, in particular, increased activations in somatosensory regions.

Study 2 investigated behavioral and neural correlates of individualized self-criticism (SC) and self-praise (SP). Previous findings with a similar paradigm reported increased amygdala activation during SC along with activations in prefrontal self-referential and emotion regulative areas (DMPFC, DLPFC) in healthy subjects (Doerig et al., 2014). According to the theoretical framework by Hölzel et al. (2011), less emotional reactivity to these stimuli was hypothesized in meditators.

Behaviorally, we expected less extreme affective ratings in LTM after blocks of SC and SP. On the neural level, decreased activation in emotion processing areas (e.g. extended amygdala) were assumed, along with differences in prefrontal self-referential and emotion regulative areas. This hypothesis was formulated non-directionally, given the conflicting theories regarding emotion regulation and mindfulness (Chiesa et al., 2013), which is reflected in inconsistent findings regarding prefrontal activations in meditators (compare section 2.2.4).

Further, group differences in functional connectivity between prefrontal activations and other regions were explored during self-appraisals. Potential targets for this task-dependent connectivity analysis were hypothesized in other prefrontal or CMS and/or emotion-generative structures.

Chapter 5

Empirical studies

Study 1: Neural correlates of mindful self-awareness in mindfulness meditators and meditation-naïve subjects revisited

Submitted to a peer-reviewed journal

Authors: J. Lutz^{1,2}, A.B. Brühl^{1,3}, H. Scheerer¹, L. Jäncke², U. Herwig^{1,4}

¹ University Hospital for Psychiatry, Clinic for Psychiatry, Psychotherapy and Psychosomatics, Zurich, Switzerland

² University of Zurich, Psychological Institute, Zurich, Switzerland

³ University of Cambridge, Department of Psychiatry, Behavioural and Clinical Neuroscience Institute, Cambridge, Great Britain

⁴ University of Ulm, Clinic for Psychiatry and Psychotherapy III, Ulm, Germany

This work was supported by the SNF Project: Emotionsregulation bei affektiven Störungen - real-time fMRI neurofeedback. Project number: 320030_146972

Abstract

Mindful self-awareness is at the heart of mindfulness meditation practices and is thought to play a key role in its salutary effects. Compared to cognitive self-reference, mindful self-awareness has been related to decreased activation in cortical mid-line structures (CMS) and the amygdala, and increased activation in somatosensory regions particularly after mindfulness interventions. To what extent these patterns are already present in untrained individuals is not completely clear and no study has verified these findings in experienced mindfulness meditators.

Using fMRI, we investigated experienced mindfulness meditators (LTM, $n = 21$) and matched meditation-naïve participants (MNP, $n = 19$) during short periods of mindful self-awareness (FEEL) and self-referential thinking (THINK). Participants further rated affective states after these periods.

We report somatosensory activations and decreases in CMS regions during FEEL for both groups, with a significantly stronger decrease in prefrontal CMS in LTM. LTM further showed decreases in left prefrontal and amygdala regions, but the latter was not significantly different between groups. Groups did not report differential affective states after FEEL or THINK. Our results demonstrate neural patterns of mindful self-awareness in untrained individuals, which get more pronounced in mindfulness meditators.

Introduction

Mindfulness meditation and clinical mindfulness programs teach a non-judgmental present-moment awareness towards experiences, in particular towards sensations, feelings, and thoughts (Baer et al., 2006; Kabat-Zinn, 2003). Mindful awareness of such self-related processes can be contrasted with cognitive self-related functions, which create self-knowledge and a coherent sense of self over time (Gallagher, 2000). Indeed, most theories of different aspects of the self distinguish a present-moment, experiential self from cognitive, self-defining functions (Damasio, 2000; James, 1890; Neisser, 1988; Northoff and Bermpohl, 2004).

These forms of self-related processes are also relevant for clinical psychology. Research suggests that a strong cognitive self-focus might be related to pathological forms of self-reference, like increased negative mood (Mor and Winquist, 2002), rumination (Killingsworth and Gilbert, 2010; Nolen-Hoeksema et al., 2008) and depressive symptoms (Northoff, 2007). In contrast, present-moment self-awareness has been linked to more adaptive self-processing and less rumination (Baer, 2009; Jain et al., 2007), thus illustrating a fundamental mechanism through which mindfulness training could exert its salutary effects on mental health (Gu et al., 2015).

On the neurobiological level, cognitive self-reference has been linked to brain activations in cortical mid-line structures (CMS) (Farb et al., 2007; Herwig et al., 2010; Northoff et al., 2006), and aberrant activity in these regions were related to depression in self-referential tasks (Lemogne et al., 2012) and during rest (Whitfield-Gabrieli and Ford, 2012). There is evidence that mindfulness training changes neural correlates of self-referential processes (Brewer et al., 2011; Hölzel et al., 2011; Lutz et al., 2016; Tang et al., 2015), however it is built on few studies (Tang et al., 2015). One study found that mindfulness training in the form of a 8 week mindfulness-based stress reduction program (MBSR) lead to altered neural processes during self-reference. MBSR participants showed reliably different neural activations between mindful self-awareness of general trait adjectives (experiential self) compared to cognitive self-evaluation of the same stimuli (narrative self), namely a shift away from CMS towards right sensory cortex activations during the experiential compared to the narrative self-focus (Farb et al., 2007). In meditation-naïve subjects, such a shift was less pronounced and Farb et al. (2007) concluded that subjects without mindfulness training probably did not enter a mindful self-awareness reliably different from cognitive self-reference.

Our group reported more differences between mindful self-awareness (here called FEEL) and cognitive self-related thoughts (here called THINK) in participants without mindfulness training (Herwig et al., 2010). The design did not involve stimuli and employed shorter blocks, in order to facilitate mindful self-aware states. Results revealed reduced activations during FEEL compared to THINK in the pre-frontal CMS (BA 9) and the

amygdala region, along with activations in somatosensory areas. All these effects were only reliably reported after MBSR training by Farb et al. (2007). Other divergent findings for mindful self-awareness compared to cognitive self-reference between in meditation-naïve participants were: Increased (Farb et al., 2007) versus decreased (Herwig et al., 2010) activation in the left DLPFC, and regions only reported in one study (activation in right DLPFC: Farb et al. 2007, activation in DMPFC: Herwig et al. 2010).

Convergent results were reported for rostral MPFC and PCC clusters. See Appendix B, Table B.2 for an overview of the most important findings per region.

To resolve these partial contradictions about how mindful self-awareness is processed in the brain without mindfulness training, a replication of the aforementioned findings in meditation-naïve subjects is warranted. The practice related changes in these networks are reported for participants of an MBSR course. Studying mindful self-awareness in more experienced mindfulness meditators would allow to verify the reported practice related changes in these networks after an MBSR course. To our knowledge, no study has looked at differential neural activations of these two self-modes in longer-term, regular mindfulness meditators.

The current study therefore aimed to validate the extend to which meditation-naïve subjects show differential neural correlates between FEEL and THINK and to directly compare their activations to mid-to-long-term meditators. To this end, we used an adapted version of Herwig et al.’s experiment, and analyzed whole-brain activations in meditation-naïve participants and mid-to-long-term meditators. Most importantly, we directly compared whole-brain analysis between groups to reach conclusions about statistically significant group differences. Based on previous findings, we hypothesized decreased activation in CMS and amygdala, and increased sensory cortex and posterior insula activation in both groups during the FEEL condition, while we also expected to find differences between the groups in these regions and the left prefrontal cortex.

Materials and methods

Subjects We recruited 22 mid-to-long-term meditation practitioners (LTM, ages: 28-67, $Mean = 47$, $SD = 11.11$, 10 female). LTM had at least 3 years of meditation experience with a minimum of 1 year in Vipassana, a current practice of at least 1 hour per week and retreat experience in Vipassana (minimum duration 3 days). The group had an average of 4862 lifetime practice hours in Vipassana or related open monitoring meditation practices (Lutz et al., 2008).

We matched LTM with 22 nearly or completely meditation-naïve participants (MNP, ages: 29-64, $Mean = 45.45$, $SD = 10.94$, 8 female) for age, gender, years of education, highest degree, general field of occupation, and a short German version of an intelligence test (Mehrfachwahl-Wortschatz-Intelligenztest, Lehrl 1977). Meditation experience was

assessed in a structured self-report screening, for full disclosure of meditation experience in both groups see Appendix A, Sample characteristics.

All subjects were right-handed according to a handedness questionnaire (Annett, 1970), with no prior or current neurological or psychiatric illnesses (self-report). Further exclusion criteria were intake of medication (except for oral contraceptives), psychotropic drugs, regular consumption of alcohol >6 units/week, cigarettes >0.5 pack/day and general contraindications against MRI examinations. The study was approved by the ethics committee of the canton of Zurich and conducted in compliance with the Declaration of Helsinki (World Medical Association, 1992). All participants gave written informed consent and received financial compensation.

Subjects with more than 1.5 mm of head movement in one direction were excluded from further analysis, resulting in 40 subjects (LTM=21, MNP=19). For an overview of the analyzed sample's sociodemographic data see Table 5.1. The analyzed sample still fulfilled our matching criteria.

Table 5.1: Sociodemographic variables of subjects included in fMRI analysis.

	MNP ($n = 19$)		LTM ($n = 21$)		LTM >MNP	
	M	SD	M	SD	Statistic (df)	p
Age	45.32	10.67	47.05	11.39	$t(38) = -.49$.62
Gender (f/m)	9/10		8/13		$\chi^2(1) = .07$.79
Education (years)	18.21	3.91	18.94	4.56	$t(38) = -.52$.61
IQ (MWT-B)	122.32	13.59	118.48	13.44	$t(38) = .90$.38

Abbreviations MWT-B Mehrfachwahl-Wortschatz-Intelligenz-Test Version B

Image acquisition Scanning was performed at the University Hospital of Psychiatry (Zurich, Switzerland) using a 3-T Philips Intera whole-body MR unit equipped with an Philips SENSE head coil. For each participant, 370 echo-planar whole-brain images were acquired (repetition-time (TR)/echo-time (TE): 2000/25 ms, 30 sequential axial slices, slice thickness: 3.0 mm, gap 1.1 mm, field of view (FOV): 240x240 mm, matrix 80x80 voxel, resulting voxel size: 3x3x3 mm, SENSE-factor: 2.0). The first four scans were discarded due to T2 saturation effects. Further, we acquired a T1-weighted high-resolution image (TR/TE 6.73/3.1 ms; voxel size 1x1x1 mm, 145 slices, axial orientation).

Questionnaires Within a week before scanning, participants completed a set of questionnaires via online investigation tool (Unipark, QuestBack).

Of particular interest for this study were *trait mindfulness* assessed by the Five Facets Mindfulness Questionnaire (Baer et al., 2006, German version: Translation by Ströhle et al., 2010, KIMS-D-Items, 2010; Michalak et al., 2008), and *depressive symptoms* assessed by the *Zung Self-rating Depression Scale* (SDS, Zung, 1965, German version:

Zung, 2005). Further, we assessed the ability to identify and describe emotions with the Toronto Alexithymia Scale (TAS, Taylor et al., 1985, German version, Bach et al., 1996) and participant’s sociodemographics, and experience with meditation and related techniques.

Before scanning we assessed participant’s affective state by administering the Positive and Negative Affect Schedule PANAS (Watson et al., 1988, German version Krohne et al., 1996). After scanning, participants were asked about general experience during scanning, how successfully they thought they completed the task and whether they experienced the FEEL condition mostly verbally (i.e. labeling their experience) or non-verbally (simply experiencing). Answers were given on a 9-point Likert scale.

fMRI experiment The paradigm is based on an established paradigm from our group (Herwig et al., 2010) on different modes of self-reference. Conditions were 12 s of cognitive self-reflection (THINK) or mindful self-awareness (FEEL), displayed in pseudo-randomised order, and interspersed with blocks of REST. Participants were instructed to: *“think about yourself, reflect who you are, what you do, like, etc.”* (for the THINK-condition) or *“Feel into yourself, simply be aware of body sensations and/or emotions in this moment”* (for the FEEL-condition) and during REST *“do nothing specific, just await the rating/distractor”*. Simple visual symbols ▲ ▼ indicated the respective task, and were followed by either an affective rating or a distractor task (Figure 5.1 A).

Affective ratings were acquired to gain insight into subjective experience during the task and potentially reveal group differences. Participants indicated how they felt on a discrete scale with the Self-Assessment Mannikins as 5 anchor points (Bradley and Lang, 1994). The scale was coded in steps of 1, ranging from -250 (= Mannikin very unhappy) to 250 (=Mannikin very happy) with 0 for neutral (Figure 5.1 B). Ratings had to be given within a maximal time window of 6 s, using a track ball (Current Designs, Philadelphia, USA). To ensure participants would not mis-identify the affective rating as the main goal of the study, they were instructed to spontaneously answer the question “How do you feel in this moment?” but focus on the THINK and FEEL task. As we wanted to prevent participants from potentially entering a permanent meta-aware state by giving affective ratings, we pseudo-randomly alternated affective ratings with a simple distractor matching task, where participants had to click on a presented Mannikin.

A randomly jittered baseline period (1-3 s, mean 2 s) separated the trials. There were twelve trials per condition in a single run. Total scan time was 12 min 20 s. Subjects completed a short training run before scanning. The task was programmed with PresentationTM, Neurobehavioral Systems, USA and presented via digital goggles (Resonance Technologies, Northridge, CA, USA).

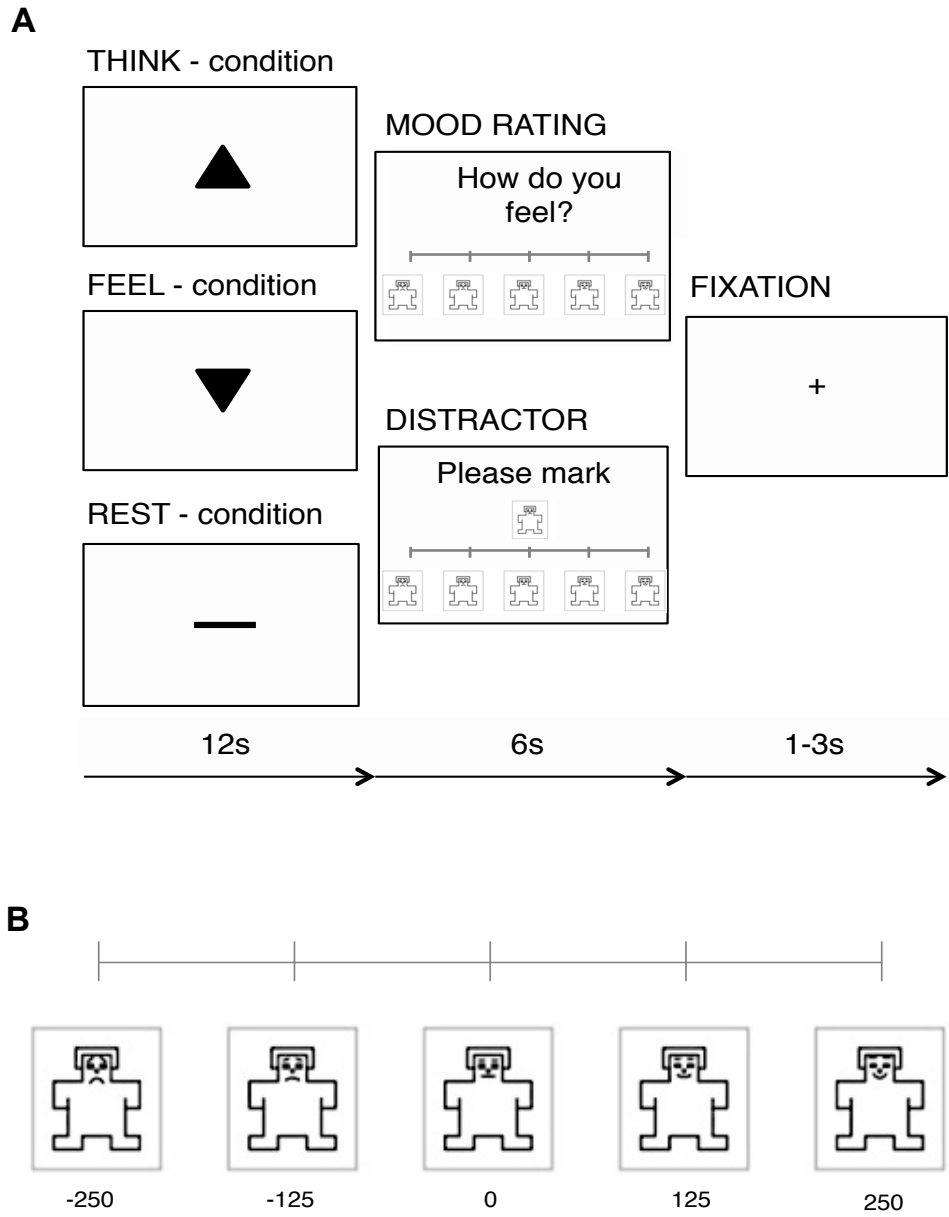


Figure 5.1: A) Schematic representation of a trial sequence including times of presentation. B) close up of the discrete affective rating scale with Mannikin's as anchor points. Values corresponding to the Mannikin's are indicated but were not visible to the participants.

Image pre-processing and analysis We used the FSL software toolbox (FMRIB's Software Library, Smith et al., 2004) for preprocessing and statistical analysis of the imaging data.

Preprocessing of the functional data included motion correction (MCFLIRT, Jenkinson et al., 2002), non-brain removal (BET, Smith, 2002), spatial smoothing (full-width half-maximum) with a Gaussian kernel of 6 mm, grand-mean intensity normalisation (FILM prewhitening, Woolrich et al., 2001) and highpass temporal filtering (cutoff period 100 s).

Pre-processed functional images were spatially registered to each subject’s skull-stripped high-resolution anatomical image using a boundary-based registration algorithm (BBR, Greve and Fischl, 2009). Normalisation of the high resolution structural image to the standard space (Montreal Neurological Institute (MNI)-152 template) was carried out using linear registration with 6 degrees of freedom (FLIRT, Jenkinson and Smith, 2001, Jenkinson et al., 2002) and further refined using FNIRT nonlinear registration with 12 degrees of freedom (Andersson et al., 2007).

Whole-brain *analysis* was conducted using the standard general linear model (GLM) approach, implemented in FEAT (FMRI Expert Analysis Tool) Version 6.00.

On the subject level, a fixed-effect model included task regressors (THINK, FEEL) and their temporal derivatives, convolved with a canonical double-gamma hemodynamic response function. Extended movement regressors were entered as nuisance regressors (6 motion parameters including their derivatives (+6) and the squares of the parameters and derivatives (+12)). Affective rating and distractor task periods (modeled as boxcars with reaction time of the trial as duration) were entered as regressors of no interest.

Z (Gaussianised t) statistic images were calculated for THINK and FEEL against implicit Baseline (B) and for the direct comparison FEEL>THINK (and THINK>FEEL). Implicit baseline consisted mainly of the 12 REST blocks.

Group-level analysis was carried out using a mixed-effects model implemented in FLAME (FMRIB’s Local Analysis of Mixed Effects, Beckmann et al. 2003, Woolrich et al. 2004, Woolrich 2008). In a single model, we computed mean activations and deactivations in MNP, mean activations and deactivations in LTM, and the contrasts between the groups (MNP>LTM and LTM>MNP, respectively). The resulting whole-brain statistic images were thresholded and FWE-corrected using clusters determined by $z > 2.3$ and a cluster significance threshold of $p < 0.05$ (based on Gaussian Random Field Theory) (Worsley, 2001). To inquire the influence of meditation training, we exploratively added regressors for total life-time meditation hours and a measure of practice intensity, as described by Fox et al. (2012) to the LTM GLM model. To comprehensively compare our results with inconsistencies in previous studies by Herwig et al. (2010) and Farb et al. (2007), we additionally created independent ROI for the left amygdala and DLPFC, right secondary somatosensory cortex (SII) and posterior insula (see Appendix B, Figure B.1). Results are only reported qualitatively (Appendix B, Table B.3).

Analysis of affective ratings Behavioral analysis is based on the 40 included subjects. Three subjects missed one rating.

Affective ratings were correlated on the subject level (ICC1 72.73%, calculated using the multilevel package (Bliese, 2013)), thus the nested data structure had to be taken into account. We formulated a linear mixed model to explain the relation between rating and the fixed effects group (MNP, LTM) and condition (FEEL (reference level), REST and THINK). We determined the random effects structure by comparing model fits between

random intercept per subject and random intercept random slope for condition per subject. Adding the random slope significantly improved model fit compared to the intercept only model ($\chi^2(5) = 33.22, p < .001$). Adding an interaction for group with condition did not improve model fit ($\chi^2(2) = 0.38, p = .83$).

Analysis of the final model was conducted in RStudio (Integrated development environment for R, RStudio, 2012), using the lme4 library (Bates et al., 2014) with the bootstrap method for calculating 95% confidence intervals.

Results

Questionnaire results and task success Groups only differed in two of the five facets of mindfulness as measured with the FFMQ: LTM scored significantly higher for *observe* ($t(38) = 2.09, p = .047$) and *non-react* ($t(38) = 2.76, p = .0093$). Further they did not differ in their ability to report feelings (TAS) or in their level of depressiveness (SDS) (Appendix A, Table A.6).

Mean level of depressiveness was 30.45 (*range* : 22 – 51), and corresponded to the normal range (20-44) except for one subject in the LTM group who scored 51, which corresponds to the mildly depressed range. This subject in the LTM group did not report a depressive phase but had stopped smoking recently. Analyses were computed with and without this subject, which did not change the results.

SDS and FFMQ had good internal consistency in our full sample (0.89 for total FFMQ and 0.82 for SDS). Both groups reported similar levels of positive and negative affect before scanning. After scanning, they indicated similar levels of comfort during the scan as well as perceived task success and easiness to get in or out of the two conditions (Appendix B, Table B.1). LTM however reported significantly less verbal labeling during the FEEL condition (Difference >1 point on a 9-point Likert scale, $t(37)=2.26, p=.030$).

Affective rating Mean mood rating during the scan across all subjects and conditions was 128.95, which represents an overall slightly positive mood on our Self-Assessment Mannikin’s scale.

In the linear mixed effect model, condition did not significantly predict affect: Compared to FEEL ($b = 126.15, 95\% \text{ CI } [92.53, 159.93]$), neither THINK ($b = 131.5524, 95\% \text{ CI } [101.68, 161.85]$) nor REST ($b = 129.4651, 95\% \text{ CI } [95.89, 159.87]$) lead to different affective ratings. Further, group did not predict overall affective ratings ($b = 0.76, 95\% \text{ CI } [-41.74, 43.62]$) (Figure 5.2).

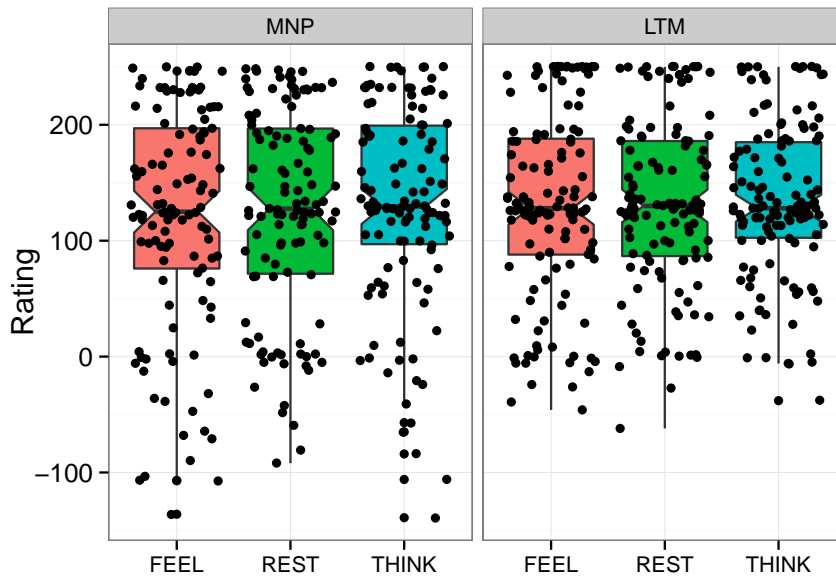


Figure 5.2: Affective ratings after the conditions FEEL, REST, and THINK. Boxplots and underlying data are visualized for meditation-naïve participants (MNP) and meditators (LTM) using ggplot 2 (Wickham, 2009). Lower and upper “hinges” correspond to the first and third quartiles, whiskers extend to $1.5\times$ the inter-quartile range.

Whole-brain results during self-related processing Single group results for FEEL>THINK are displayed in Figure 5.3: In both groups, we found significantly *reduced* CMS activations in prefrontal regions (BA 10), the anterior cingulum (BA 25) and occipital regions covering parts of the precuneus/PCC (BA 23/31) and cuneus (BA 18). *Activation* clusters present in both groups were found in bilateral parietal regions (supramarginal gyrus/secondary somatosensory cortex), and a more anterior part of the precuneus (BA 7). Only LTM displayed significantly lower activation the left inferior prefrontal area including Broca’s area, and in bilateral hippocampus/amygdala and caudate regions. Furthermore, significant activations in the bilateral posterior insula, posterior DMPFC (pre-supplementary motor area (SMA)) and right DLPFC were only found in LTM during FEEL>THINK.

As we found no group difference during the THINK condition (Table 5.3), we could directly compare the groups in this contrast. Direct comparison revealed that CMS reductions were significantly larger in LTM and that the reduction in the left inferior prefrontal area (only found in LTM) was also significantly different from MNP on the group level (Table 5.2, and Figure 5.4).

Note that the other discussed regions which were significantly deactivated in LTM only (amygdala, caudate) or significantly activated in LTM only (insula, right DLPFC), were not significantly different in the group comparison.

Although there was no group difference in the THINK condition, we wanted to confirm these results in the FEEL>B contrast. We found similar reduced activations in posterior CMS regions in both groups. Again, the group comparisons resulted in significantly higher prefrontal CMS activations, and higher activation in left-sided inferior frontal areas corresponding to Broca’s area in MNP compared to LTM (Table 5.3). Also, we found reduced activation in amygdala/hippocampus and activations in insular regions for LTM only, but again they did not result in significant differences in the direct group comparison. In the FEEL>B contrast, MNP showed reduced activation in the right DLPFC, which was significant in the direct group comparison (Appendix B, Figure B.2). The LTM results did not show a relation with meditation experience. The explorative independent ROI analysis confirmed our observations from the whole-brain results qualitatively (Appendix B, Table B.3).

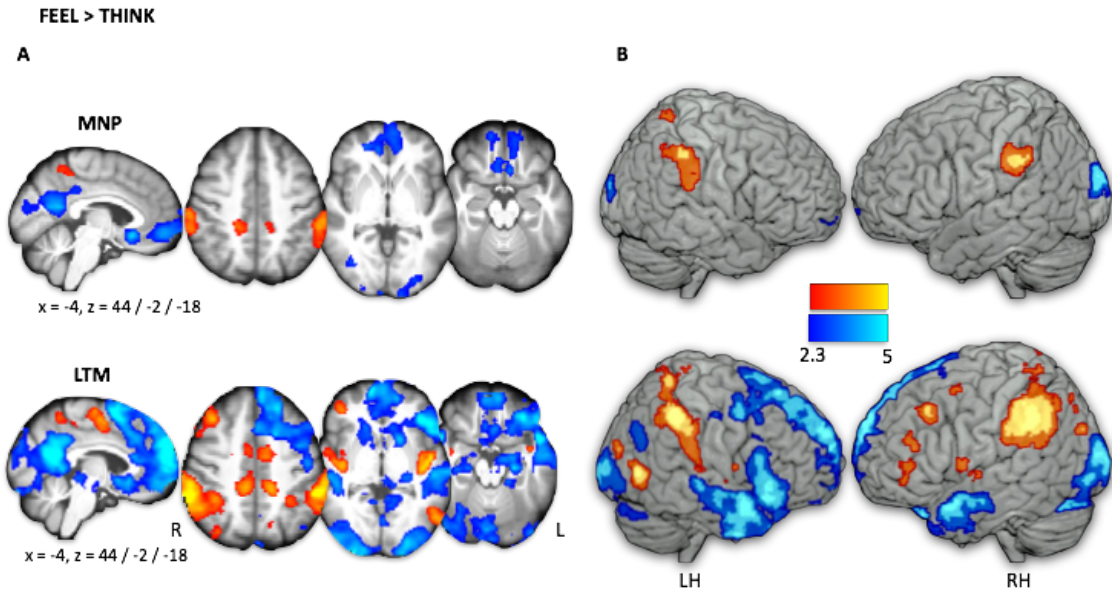


Figure 5.3: Increased neural activations (red) and decreased neural activations (blue) during FEEL>THINK. Probability maps depict significant results for meditators (LTM), meditation-naïve participants (MNP) in A) sagittal and axial slices and B) in a surface-rendered view using the ch2better template and MRIcron (www.mricron.com/mricron/install.html). L left, R right, H hemisphere.

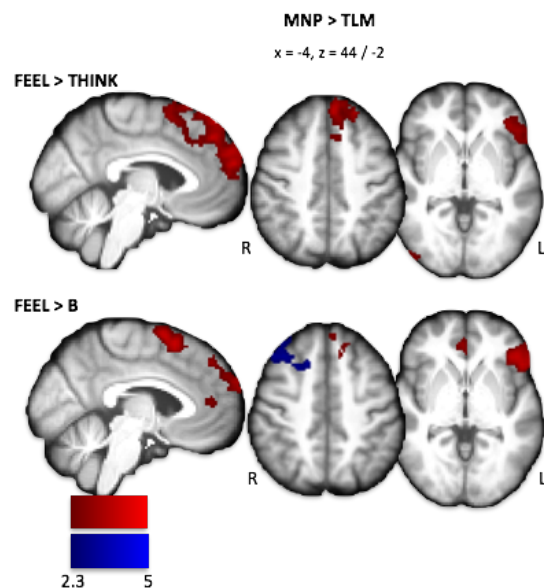


Figure 5.4: Direct group comparisons of neural activations during FEEL>THINK and FEEL>baseline (B) E. Higher activations in meditation-naïve participants (MNP) compared to meditators (LTM) are depicted in red, lower activations in blue. L left and R right.

Table 5.2: Group comparison of brain activations during FEEL compared to THINK

Brain regions		BA	<i>n</i> of Voxels	Coordinates			<i>t</i>	<i>p</i>
				<i>x</i>	<i>y</i>	<i>z</i>		
<i>FEEL>THINK - Activations</i>								
<i>MNP>LTM</i>								
Frontal Pole	M/L	6 (DMPFC)	4050	-8	60	20	4.88	< .0001
Superior Medial Frontal	M/L	6		-14	30	60	4.56	
Inferior Frontal	L	45 (Broca)	1293	-60	26	-4	4.71	< .001
Cerebellum	R	Culmen	839	32	-64	-26	3.84	.012
<i>LTM>MNP</i>								
No sign. difference								

Clusterwise corrected with $p = .05$ (FWE) at whole-brain level.

Abbreviations LTM mid-to-long-term meditators, MNP meditation-naïve participants, BA Brodmann area, DMPFC dorso-medial prefrontal cortex, R right, L left, M medial

One indentation: absolute cluster maxima, two indentations: local clustermaxima.

Stereotaxic coordinates based on the human atlas of MNI, BA based on Talairach Daemon labels in FSL view.

Table 5.3: Group comparison of brain activations during FEEL and THINK

Brain regions		BA	<i>n</i> of Voxels	Coordinates			<i>t</i>	<i>p</i>
				<i>x</i>	<i>y</i>	<i>z</i>		
<i>FEEL>B</i>								
<i>MNP>LTM</i>								
Superior Medial Frontal	M	6 (DMPFC)	666	-6	8	64	4.69	.039
Paracingulate	M/L	9	1446	-14	52	16	4.32	< .001
Anterior Cingulum	L/M	32		4	44	0	4.10	
Frontal Pole	L/M	9/10		-12	64	28	3.85	
Inferior Frontal	L	45/44(<i>Broca</i>)	1154	-42	30	2	4.72	.0017
<i>LTM>MNP</i>								
Middle Frontal	R	8/9	752	44	32	40	3.4	.0215
<i>THINK>B</i>								
No sign. group differences								

Clusterwise corrected with $p = .05$ (FWE) at whole-brain level.

Abbreviations LTM mid-to-long-term meditators, MNP meditation-naïve participants, BA Brodmann area, DMPFC dorso-medial prefrontal cortex, R right, L left, M medial

One indentation: absolute cluster maxima, two indentations: local clustermaxima.

Stereotaxic coordinates are based on the human atlas of MNI, BA are based on Talairach Daemon labels in FSL view.

Discussion

This study aimed to elucidate neural correlates of short periods of mindful self-awareness (FEEL) in meditators (LTM) and meditation-naïve participants (MNP).

The question was, to what extend these groups would show typical neural correlates of mindful self-awareness and in which areas they would differ. To bring the results in perspective, we compared behavioral measures regarding task experience and psychometric measures.

Affective ratings and questionnaire results We found little difference between groups regarding their subjective experiences during the task. Affective ratings after THINK and FEEL did not differ and they reported similar task success and ease of initiating the conditions. However, MNP reported a bigger verbal component during mindful self-awareness. Labeling of experience is a common practice in formal mindfulness training (Creswell et al., 2007), particularly in introductory courses (Brown et al., 2007). It would make sense that meditation-untrained participants use a labeling strategy during a mindful self-awareness task. Thus, we interpret the higher verbal component not merely as mind-wandering, but as (mindful) labeling of present moment experience (Lieberman et al., 2007), especially since task success was rated similarly. Of course, we can not rule out that groups differed in task success, but had different standards for rating their success: LTM might have compared it to “good” meditation while MNP have less reference for mindful states or MNP might simply be less aware of mind-wandering, and consequently

be less reliable to report success during FEEL (Grossman, 2011). However, we think that for short periods of 12 s, groups might still be comparable in their ability to report their experience. In fact, MNP did observe and report increased levels of verbal labeling during FEEL. Overall, the fact that experience during our task was similar renders our group comparison more meaningful, and implications for mindfulness-related clinical therapies more relevant.

Regarding our questionnaire results, LTM only scored higher in two of the five facets of trait mindfulness and we found no differences in levels of alexithymia. Reasons could be a limited comparability of self-report mindfulness questionnaires between meditators and non-meditators (Grossman and Van Dam, 2011; Van Dam et al., 2009) or the high IQ and education of our samples which could decrease differences between the groups (Baer et al., 2008).

Neural correlates of mindful self-awareness in meditation-naïve and mindfulness meditators The FEEL condition revealed reduced activations in CMS in both groups in prefrontal regions and the precuneus/PCC and cuneus. This pattern confirms our hypothesized down-regulation of cognitive self-referential CMS regions associated with the default mode network and mind-wandering (Gusnard et al., 2001) during mindful self-awareness. The direct group comparison revealed that reductions in prefrontal CMS regions were significantly larger and more extensive in LTM. This is consistent with the findings of Farb et al. (2007), who observed more pronounced deactivations in participants of an MBSR course compared to meditation-naïve subjects. Still, reduced mid-line prefrontal and PCC activations during FEEL were also observed in MNP, similar to results of Herwig et al. (2010). Thus, while mindfulness training seems to increase typical mindfulness-related CMS reductions and the neural distinction between mindful self-awareness and cognitive self-reference, we observed the basic pattern of decreased CMS activations already in mindfulness-naïve participants.

With regards to reported DMPFC activations in the previous study by (Herwig et al., 2010), we note that LTM showed increases in a dorsal DMPFC/pre-SMA region just adjacent to the described reductions during FEEL. Thus, we have to be precise in describing the exact loci of mid-line findings in self-referential tasks. The fact that DMPFC activations were only reported by Herwig et al. (2010) and replicated in LTM in the current study indicates that they might be related to the purely internal task design, as opposed to self-referential tasks using external stimulation (trait-adjectives). The exact functions of the pre-SMA are still being investigated, but apart from motor functions, it has been linked to internally guided action, action intentions and monitoring (Nachev et al., 2007) or to the salience network regulating the default mode network (Bonnelle et al., 2012). Both interpretations would fit, as our purely internal task is close to actual mindfulness practice, but consequently demands more intention, attention and monitoring from participants, and as we found distinct SMA activations during FEEL in LTM only

who also exhibited larger reductions in typical default mode regions during this condition. Only LTM displayed significant reductions in the *left inferior prefrontal areas* including the language related Broca’s area, which has also been linked to affective labeling tasks in meditation-naïve samples (Lieberman et al., 2007; Torrisi et al., 2013). This could correspond to the self-reported difference in verbal experience during FEEL between the groups, indicating less verbal labeling of inner experience or inner speech during self-reflective processes (Morin and Michaud, 2007) in LTM.

Regarding the hypothesized reductions in *amygdala/hippocampus* areas, associated with emotional arousal (Phan et al., 2003), group differences were less clear. In the whole-brain, LTM showed significant reductions during mindful self-awareness, but the direct group comparison revealed no significant differences between groups. We did not find significant amygdala reductions in meditation-naïve participants as reported by Herwig et al. (2010). If the emotion-balancing effect of mindful self-awareness is similar but smaller in meditation-naïve participants, differences in sample size could explain the current null finding. Herwig et al. (2010) analysed 27 subjects, while the current study had only 19, and the study by Farb et al. (2007) only 16 meditation-naïve participants. Mindfulness related affect-labeling tasks, have already demonstrated regulative effects on the amygdala in meditation-naïve participants (Lieberman et al., 2007), particularly related to high trait mindfulness (Creswell et al., 2007; Modinos et al., 2010). But other factors might be more relevant in untrained participants, such as levels of depressiveness (Way et al., 2010).

We found no group differences regarding activations in right *somatosensory and posterior insula* during FEEL. Activations in these regions were reported by Herwig et al. (2010), but only in mindfulness trained participants by Farb et al. (2007). Our results indicate that activations in regions associated with somatosensory attention and present moment awareness (Bauer et al., 2014; Critchley et al., 2004) are already found in meditation-naïve participants. Similarly, we did not find a group difference in parietal regions, as described by Farb et al. (2007) who found bilateral activation in meditators and only left-sided parietal activation in meditation-naïve. In line with Herwig et al. (2010) we find bilateral parietal activation in both groups. These inconsistencies in somatosensory and parietal regions might be related to the verbal stimulus driven design of Farb et al. (2007)’s experiment, which compared to our design might have been harder for meditation-naïve participants, and might have covered first mindfulness-related activations.

To sum up, we did not find previously suggested significant group differences in amygdala, insula and somatosensory cortex during mindful self-awareness. But we confirm reduced prefrontal CMS activations which mindfulness trained subjects showed to a significantly larger degree. We further identified significant reductions in left inferior prefrontal activation in this group, probably reflecting a smaller verbal component during mindful self-awareness.

Clinical relevance Mindful self-awareness was associated with decreased activation in prefrontal and posterior CMS and in the amygdala/hippocampus formation in LTM. This suggests that mindful states in general, but particularly in meditators, are associated with decreased activation in regions associated with rumination and being caught up in thought (Brewer et al., 2013) and emotional arousal (Phan et al., 2003). Similar associations were found in healthy individuals during rest, where amygdala activation was negatively related to trait mindfulness (Way et al., 2010). And Hölzel et al. (2009) demonstrated reduced grey matter density in the amygdala associated with stress reduction after MBSR training. Here we add further evidence that mindful awareness is associated with emotionally-balanced, de-centered self-referential processing.

Limitations and future research Our observations regarding training induced changes in LTM must be taken with a grain of salt, as we found no association between life-time hours of meditation or intensity of meditation training and LTM results. The highly diverse experience concerning all mindfulness-related practices in our relatively small LTM sample might have made it difficult to detect such significant developmental trajectories in our data. As a group, however, our LTM results are in line with previous findings after MBCT training (Farb et al., 2007). However, neither study is longitudinal. Thus, conclusions about mindfulness training and associated changes in self-related processes need to be backed up in longitudinal studies (Davidson, 2010). Related to our cross-sectional design, we also can not rule out that demand characteristics or subject selection affected the result; i.e. meditators might have consciously or unconsciously tried to conform to the image associated with meditators, or meditators might have differed from meditation-naïve participants in personality-related factors in the first place.

Our conclusions on significant brain activations are built on whole-brain FWE error correction using random field theory. With regards to affective sciences, such corrections are often employed to avoid both Type I and Type II errors (Lieberman and Cunningham, 2009). Further, our analysis of previous studies lead to a concise set of regions of interest, which we explored in our current sample. Still, meta-analysis are needed to verify the current knowledge of brain activation during mindful self-awareness. Finally, we note that the findings regarding the amygdala are tentative, as activations in this area are challenging to measure with fMRI (Lipp et al., 2014), and recent research suggests a strong influence of blood flow changes in a nearby vessel, which is related to activations in other, distant brain regions (Boubela et al., 2015). However, this finding was mainly based on external emotional stimuli, which were not employed in our task. Still, in a further step, explorations of functional networks during mindful self-awareness should complement our results, to overcome the limits of studying local brain activation.

As mentioned, longitudinal studies are needed to further elucidate developmental trajectories of self-related processes related to mindfulness training. Such studies would further allow us to extend our limited knowledge on mindful self-awareness to more diverse

samples and clinical populations. By studying neural and behavioral differences during states of mindful self-awareness, we could potentially predict who will profit most from mindfulness interventions. Integrating the results from our study and previous studies, we suggest potential neural markers in the CMS, amygdala/hippocampus regions, left inferior prefrontal, and somatosensory areas.

Study 2: Altered processing of self-related emotional stimuli in mindfulness meditators

Neuroimage, 2016

Authors: J. Lutz^{1,2}, A.B. Brühl^{1,3}, N. Dörig², H. Scheerer¹, R. Achermann², A. Weibel², L. Jäncke², U. Herwig^{1,4}

¹University Hospital for Psychiatry, Clinic for Psychiatry, Psychotherapy and Psychosomatics, Zurich, Switzerland

²University of Zurich, Psychological Institute, Zurich, Switzerland

³University of Cambridge, Department of Psychiatry, Behavioural and Clinical Neuroscience Institute, Cambridge, Great Britain

⁴University of Ulm, Clinic for Psychiatry and Psychotherapy III, Ulm, Germany

This work was supported by the SNF Project: Emotionsregulation bei affektiven Störungen - real-time fMRI neurofeedback. Project number: 320030_146972

Abstract

Mental health benefits of mindfulness techniques are thought to involve changes in self-processing, such as decreased attachment to the self, higher self-compassion and lower emotional reactivity to inner experience. However, self-related emotion processing in regular mindfulness practitioners is not extensively studied. In the current work we investigate differential neural and behavioral correlates of self-criticism and self-praise in 22 mid-to-long-term mindfulness meditators (LTM) compared to 22 matched meditation-naïve participants (MNP).

In an fMRI experiment, participants were presented with blocks of individually selected positive (self-praise, SP), negative (self-critical, SC), negative but not self-critical (NNSC), and general, neutral (NT) adjectives, and reported their affective state after the blocks. On the neural level, both SP and SC yielded more activation in the dorso-medial prefrontal cortex (DMPFC) in LTM compared to MNP. Activation in this region correlated positively with non-react scores of the Five Facets Mindfulness Questionnaire (FFMQ) and showed decreased functional connectivity to posterior midline and parietal regions in LTM compared to MNP during both self-related appraisals. Further, we found evidence for emotional reactivity in LTM on the neural level, particularly during SP. On the behavioral level, a mixed effects analysis revealed significantly higher differences in affective ratings after blocks of SC compared to SP in MNP compared to LTM.

Differences in DMPFC activation and affective ratings point towards increased awareness, potentially mindful regulation of SC and SP in LTM, while decreased connectivity to other regions of the default mode network could reflect a decreased self-focus in this group. As such, our results illustrate differences in self-related emotional processes in meditators and offer clinically relevant insights into mechanisms of mindful emotion regulation when facing self-criticism and self-praise.

Introduction

Self-related emotional processes are often disturbed in affective disorders. For example, depressed patients display a stronger and more negative self-focus (Greenberg and Pyszczynski, 1986; Joormann and Gotlib, 2010; Northoff, 2007) and increased rumination about negative aspects of the self (Nolen-Hoeksema et al., 2008), while excessive self-critical thinking represents a vulnerability factor to depressive symptoms (Sherry et al., 2012). Despite the fundamental role of such self-related processes for mental health, research has only started to investigate disturbances of the self in affective disorders and possible mechanisms of change (Northoff, 2007).

At the same time, concepts like mindfulness and self-compassion have been increasingly incorporated into psychotherapy programs with the goal of facilitating healthier self-related processes (Keng et al., 2011; Baer et al., 2006). Mindfulness is often defined as *purposeful attention on momentary experiences in a non-judgemental way* (Brown et al., 2007; Kabat-Zinn, 1990). Such a mindful state can be trained through meditation techniques and is believed to ultimately increase mindful behavior in everyday life (Kiken et al., 2015), for example in the facets: *acting with awareness, non-judging and non-reacting* to inner experiences, *describing experiences, and observing* (Baer et al., 2006). In relation to self-referential processes, a mindful present-moment focus can lead to a less attached and biased relation towards the self (Bishop et al., 2004) and less concerns with self-esteem (Brown et al., 2007). Moreover, self-related emotions might be faced less judgmentally and in a more accepting (Linehan, 1994), self-compassionate way (Neff, 2003; Thompson and Waltz, 2008). Thus, mindfulness and self-compassion presumably lead to better emotion regulation skills with regards to self-related emotions, like dampening the negative effects of excessive self-critical thinking (Bishop et al., 2004; Hollis-Walker and Colosimo, 2011). Similarly, theoretical frameworks of mindfulness and neurobiological correlates propose changes in self-related functions as key mechanisms of salutary effects of mindfulness (Hölzel et al., 2011; Vago and Silbersweig, 2012).

Despite these proposed mechanisms and the clinical necessity to understand mindfulness-related changes in self-related processes, research in this area is scarce, particularly regarding the neural level (Hölzel et al., 2011). One influential study on mindful self-referential processing after a mindfulness course found a shift from a narrative self-reference, which they associated with cortical mid-line areas like the dorso-medial prefrontal cortex (DMPFC) towards a more experiential body awareness (Farb et al., 2007). However, other studies report increases in mid-line areas related to mindfulness, as during mindful affect labeling (Creswell et al., 2007; Lieberman et al., 2007), mindful self-awareness (Herwig et al., 2010), and mindful perception of emotional stimuli in meditation-naïve participants (Lutz et al., 2014) and also in mindfulness meditators during mindful breathing (Hölzel et al., 2007).

Many studies on self-related processes contain a factor of decision making, i.e. participants judge whether a particular adjective describes themselves versus someone else (Northoff et al., 2006). Studying self-referential processes and particularly self-related emotions in this way involves decision making aspects, which arguably occur to a much lesser degree in every-day self-appraisals. A recent study therefore investigated negative and positive self-appraisals in the form of individual inner talk (Brühl et al., 2014). Both conditions activated the DMPFC and dorso-lateral prefrontal (DLPFC) regions, while positive appraisals showed stronger activations in emotion generative regions (amygdala/ventral striatum). This study, being close to every-day self-appraising thoughts, has high ecological validity, but the appraisals were not reported to the experimenters, thus the emotional involvement and relevance for the individual was not fully controlled. A study by Doerig et al. (2014), used self-critical stimuli that had been individually chosen and evaluated by each participant before a block-designed fMRI experiment. For self-critical stimuli, they reported neural activity in regions involved in emotion generation (anterior insula/hippocampus/amygdala formation), and bilateral frontal areas, presumably representing cognitive reappraisal of the evoked negative affect. They further reported activations in mid-line prefrontal areas for self-criticism. However, the study was limited to negative aspects of the self and no behavioral measure complemented the results.

The goal of the current study is to extend the clinically relevant but limited knowledge on mindful processing of self-related emotions. By extending Doerig et al. (2014)’s paradigm, we studied differential neural and behavioral correlates of individualized self-criticism (SC) and self-praise (SP) in meditators with experience in Vipassana and closely related mindfulness practices (Lutz et al., 2008) compared to matched meditation-naïve controls. We focused on the Vipassana tradition, because it influenced current secular, clinical programs like Mindfulness-Based Stress Reduction (MBSR) or Cognitive Therapy (MBCT) (Chiesa and Malinowski, 2011), and would potentially allow first translational insights into altered self-related emotional processes through mindfulness training.

We hypothesized that 1) mid-to-long-term, regular mindfulness meditators (LTM) would show decreased habitual emotional reactivity to emotional, self-referential stimuli (SC and SP) both by decreased activity in emotion processing areas (extended amygdala/hippocampus region) and/or differential affective experience based on affective ratings after blocks of SC and SP. Similarly, we hypothesized 2) differential activity in prefrontal, self-referential and regulative areas, mainly DLPFC and DMPFC regions. Given the mixed findings for prefrontal areas, we formulated this hypothesis non-directional. In addition, we explored neural correlations with particular aspects of trait mindfulness and differences in the functional connectivity between LTM and MNP.

Materials and methods

Subjects Mid-to-long-term meditation practitioners (LTM) were recruited via local meditation groups and personal contacts. We required meditators to have more than one year of meditation experience with at least one year of regular Vipassana training, Vipassana retreat experience and a current practice of at least one hour per week. We included 22 LTM (ages: 28-67, $mean = 47$, $SD = 11.11$, 10 female) with an average of 4'861.50 lifetime practice hours in Vipassana or closely related open monitoring meditation techniques (Lutz et al., 2008) (range 281-18325), and an average of 5971 hours (range 506-18805) when considering all meditation experience in this group (see Appendix A, for full disclosure of LTMs mindfulness-related experience and current practice).

LTM were matched with 22 nearly or completely meditation-naïve participants (MNP, ages: 29-64, $mean = 45.45$, $SD = 10.94$, 8 female), recruited via mailing lists and personal contacts. For matching statistics see Appendix A, Tables A.4 and A.5. MNP did not have a current or recent meditation practice (Appendix A, Table A.3). Matching variables were age, gender, years of education and highest degree of education, general field of occupation, and crystalline intelligence measured with Mehrfachwahl-Wortschatz-Intelligenztest (MWT-B, Lehrl, 1977).

All subjects were right-handed according to a handedness questionnaire (Annett, 1970) and without self-declared mental or neurological disorders. Further exclusion criteria were intake of psychotropic drugs, consumption of alcohol >7 units/week, cigarettes >10 units/day, or coffee (>10 cups/day) and general contraindications against MRI examinations.

The study was approved by the ethics committee of the canton of Zurich and conducted in compliance with the Declaration of Helsinki (World Medical Association, 1992). All participants gave written informed consent and received a financial compensation.

Experimental design

Questionnaires Within a week before scanning, participants completed a set of questionnaires via an online investigation tool (Unipark, QuestBack).

Of particular interest for this study were trait mindfulness and self-compassion. Mindfulness was assessed by the *Five Facets Mindfulness Questionnaire* (FFMQ, Baer et al., 2006, German version: Translation by Ströhle et al., 2010, KIMS-D-Items, 2010; Michalak et al., 2008), with the facets: 1) observing and 2) describing sensations, perceptions, thoughts and feelings, 3) acting with awareness, 4) non-judging of, and 5) non-reactivity to inner experience. For self-compassion we administered the *Self-Compassion Scale* (SCS, Neff, 2003, German version: Hupfeld and Ruffieux, 2011).

Further, we assessed the ability to identify and describe emotions with the *Toronto Alex-*

ithymia Scale (TAS, Taylor et al., 1985, German version: Bach et al., 1996), participant’s sociodemographics, and experience with meditation and mindfulness-related techniques. Before scanning we administered the *Positive and Negative Affect Schedule* (PANAS, Watson et al., 1988, German version: Krohne et al., 1996) to control for mood before scanning. After scanning, participants were asked in a structured interview about fatigue, general experience, pain, and discomfort during scanning.

Stimuli Stimuli consisted of negative and positive personality-descriptive adjectives from the groups: appearance, social aspects, transient condition, talents, and dispositions and neutral words (Angleitner et al., 1990). The construction of 52 negative and neutral adjectives has been described in Doerig et al. (2014) and has been adopted for the additional list of 52 positive adjectives in the current experiment.

Within a week before scanning, participants selected via the online investigation tool all applicable, but a minimum of six self-critical (SC) adjectives, and six negative, but not self-relevant and thus not self-critical (NNSC) adjectives from the list of negative adjectives. From the list of positive adjectives they selected all applicable, but a minimum of six self-praising (SP) adjectives. They further rated the adjectives regarding their subjective negative and positive valence (e.g. for SC-stimuli: “How negative do you perceive this trait?”) on a 5-point Likert scale ranging from “1: not at all” to “5: very much”.

For experimental stimulation, each adjective was supplemented with three synonymical adjectives from the same self-schema (compare Doerig et al., 2014).

Experiment The experiment is based on Doerig et al. (2014)’s paradigm, extended with a self-praising condition and affective ratings.

The four conditions (SC, SP, NNSC, NT) and interjacent blocks of rest were presented in pseudo-randomised order. The introduction varied depending on the respective condition (self-criticism: “I am too”; self-praise: “I am very”, negative non-self-referential: “I am not”; neutral: “it is”), followed by a fixation cross. Subsequently, the four adjectives relating to a particular self-schema were presented, separated by fixation crosses. A block lasted for 24 s. Subjects were instructed to focus on the meaning of the adjectives and any emotional response triggered by the adjectives. During the blocks of rest, subjects were asked to relax and do nothing in particular. LTM were specifically reminded to not meditate during the task or rest periods. After SC, SP, NNSC and NT blocks we acquired affective ratings and showed a fixation cross (duration: 2 s + not used affective rating time). Each condition and rest periods were presented six times, resulting in 30 blocks and a total scan time of 15 min 15 s (see Figure 5.5).

All negative, positive and neutral adjectives were presented only once. Two versions of the task were created, starting either with SC or SP. Subjects were randomly assigned to a version, each version was administered to half of the participants in each group. The

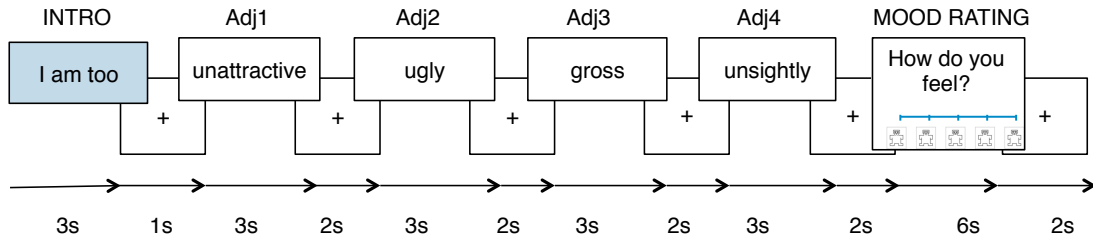


Figure 5.5: Schematic representation of one experimental block (SC condition) including times of presentation. Introduction depended on the respective condition.

task was programmed with PresentationTM, Neurobehavioral Systems, USA and was presented via digital goggles (Resonance Technologies, Northridge, CA, USA). Subjects completed a trial run with meaningless adjectives before scanning.

Affective rating As a manipulation check and insight into subjective experience during the experiment, we acquired affective ratings using a track ball (Current Designs, Philadelphia, USA) within a maximal time window of 6 s. To ensure participants would not mis-identify the affective rating as the main goal of the study, the instruction was to spontaneously answer the question "How do you feel in this moment?" but mainly focus on the task with the adjectives. Ratings were given on a discrete scale with the Self-Assessment Mannikins as 5 anchoring points (Bradley and Lang, 1994). The discrete scale was coded in steps of 1, ranging from -250 (= Mannikin very unhappy) to 250 (=Mannikin very happy) with 0 as neutral.

Since ratings of an individual were correlated (ICC1 0.53), the nested data structure had to be taken into account. We formulated a linear mixed model to explain the relation between the dependent variable rating and the fixed effects group and condition. Condition had SC as the reference level and further contained SP and the two non-self-referential conditions NNSC and NT. The group factor had two levels (LTM, MNP). Our model contained a random effect for each subject¹. Since we hypothesized group differences in ratings after self-related emotional conditions but not after non-self related conditions we further included an interaction term for group and condition. Adding the group condition interaction significantly improved model fit ($\chi^2(3) = 12.75, p = .005$). Analysis of the mixed effects model was conducted using the lme4 library (Bates et al., 2014) in RStudio (Integrated development environment for R, RStudio, 2012). ICC was calculated using the multilevel package (Bliese, 2013), 95% confidence intervals were calculated using the bootstrap method.

¹We determined the random effects structure of our model by comparing model fits between a random intercept and a random intercept random slope for subject in group. The latter decreased the model fit. Thus our final model contained a random effect for subject.

Image acquisition Scanning was performed at the University Hospital of Psychiatry (Zurich, Switzerland) using a 3-T Philips Intera whole-body MR unit equipped with a Philips SENSE head coil. With a sensitivity-encoded (Pruessmann et al., 1999) singleshot echo-planar sequence (SENSE-sshEPI), 305 T2*-weighted echo planar image volumes with blood-oxygen-level-dependent (BOLD) contrast were acquired (repetition-time (TR)/echo-time (TE): 3000/30 ms, 36 transversal slices, whole brain, slice thickness: 4.0 mm, field of view (FOV): 240x240 mm, matrix 80x80 voxel, resulting voxel size: 3x3x4 mm, orientation, SENSE-factor: 2.0). For each participant, a T1-weighted high-resolution image was acquired (TR/TE 6.73/3.1 ms; voxel size 1x1x1 mm, 145 slices, sagittal orientation, FOV: 230x225x225 mm).

Image pre-processing Preprocessing and statistical analyses were conducted with the FSL software toolbox (Oxford Centre for Functional Magnetic Resonance Imaging of the Brain, FMRIB, Smith et al., 2004). Preprocessing of the functional data included motion correction (MCFLIRT, Jenkinson et al., 2002), non-brain removal (BET, Smith, 2002), spatial smoothing (full-width half-maximum) with a Gaussian kernel of 6 mm, grand-mean intensity normalisation (FILM prewhitening, Woolrich et al., 2001) and highpass temporal filtering with a cutoff period of 100 s. Pre-processed functional images were spatially registered to each subject’s skull-stripped high-resolution anatomical image using a boundary-based registration algorithm (BBR, Greve and Fischl, 2009). Normalisation of the high resolution structural image to the standard space (Montreal Neurological Institute (MNI)-152 template) was carried out using linear registration with 6 degrees of freedom (FLIRT, Jenkinson and Smith, 2001, Jenkinson et al., 2002) and further refined using FNIRT nonlinear registration using 12 degrees of freedom (Andersson et al., 2007).

General linear model image analyses Whole-brain analysis was conducted using the standard general linear model (GLM) approach, implemented in FEAT (FMRI Expert Analysis Tool) Version 6.00. First-level analysis comprised a fixed-effect model for each subject, with box car functions for the four condition regressors (SC, SP, NNSC, NT), convolved with a canonical double-gamma hemodynamic response function including temporal derivatives. Extended movement regressors were entered as nuisance regressors (6 motion parameters including their derivatives (+6) and the squares of the parameters and derivatives (+12)). Affective rating periods (scale, modeled as boxcars with scale onset and the reaction time of the trial as duration) were entered as regressors of no interest. Z (Gaussianised T) statistic images were calculated for our contrasts of interest $SC > NT$ and $SP > NT$. For reasons explained in the behavioral results section, we did not analyze $SC > NNSC$.

Second-level group comparison of the first-level results was carried out using a mixed-effects model implemented in FLAME (FMRIB’s Local Analysis of Mixed Effects, Beckmann et al., 2003, Woolrich et al., 2004, Woolrich, 2008). The whole-brain contrasts were

thresholded and FWE-corrected using clusters determined by $z > 2.3$ and a cluster significance threshold of $p < 0.05$ (based on Gaussian Random Field Theory) (Worsley, 2001).

Conjunction and correlation analysis In a conjunction analysis between SP >NT and SC >NT we determined group difference in emotional self-referential processes independent of valence, using the conjunction null method based on the minimum statistic (Nichols et al., 2005). To further investigate group differences in our contrasts of interest, we computed Pearson correlations between facets of mindfulness that differed between groups and percent signal changes in the conjunction cluster. We further exploratively correlated percent signal change in the conjunction with total hours of practice adjusted for age (Brefczynski-Lewis et al., 2007) and with practice intensity (Fox et al., 2012). However, given the heterogeneity of mindfulness-related experience in our LTM sample we did not expect significant correlations. Functional mean activation from the cluster were extracted for each participant and converted to percentage signal change as outlined by Mumford (2007).

Psycho-physiological interaction Based on the result from the conjunction analysis, we explored differences in functional connectivity between groups during self-related emotional conditions (EMO). To this end, we collapsed SC and SP conditions into a single EMO regressor and conducted a psycho-physiological interaction analysis (PPI, Friston et al., 1997), in which the activation in the conjunction cluster (SEED) was compared to linearly detrended whole-brain fMRI activations (TARGET). In this GLM, we entered the fMRI time-series from the seed (extracted on the subject level, with the conjunction cluster transformed into the individual’s functional space) as the physiological regressor (PHYS) and the EMO regressor. Other task regressors (NNSC, NT) and confound regressors (affective ratings periods, movement) were the same as in the standard GLM analysis. To test the PPI in the generalized, most sensitive form for block designs (Cisler et al., 2014), we included separate PPI terms for the EMO conditions (PHYS×EMO) and NT (PHYS×NT) and modeled the PPI effect of interest as the contrast between these regressors (PHYS×EMO >PHYS×NT), including the analogous negative relationship (PHYS×NT >PHYS×EMO). On the group level, we compared group differences in these functional connectivity patterns (PPI LTM versus PPI MNP). In order to disentangle this slightly complex double-regression and get at the underlying linear relations between seed and target regions, we checked if regions that were significantly different in the group comparison (LTM >MNP), showed positive or negative PPI effects in the mean single group results. We applied the same statistical thresholds and FWE-correction as in the main analysis.

Results

Stimulus selection and questionnaire results Groups did not differ in the number of self-chosen SC and SP stimuli, nor in the positive (for SP) or negative (for SC) evaluation of their stimuli before the scan (Appendix C, Table C.1).

Comparing trait mindfulness, measured with the FFMQ, we found significantly higher scores for LTM only for two of five factors, namely for *observe* ($t(42) = -2.38, p = .02$) and *non-react* ($t(42) = -3.30, p = .002$). Further, LTM showed higher self-compassion (SCS) and lower alexithymia (TAS) scores compared to MNP. Both differences showed a trend but were not significant (Appendix A, Table A.6). Using a *fdr* correction for the group comparisons in all 13 questionnaire-measures, only non-react was significantly different. Both groups reported similar levels of positive and negative affect before scanning. After scanning, they indicated similar levels of comfort during the scan. There was a trend towards more reported tiredness during the scan in MNP (Appendix A, Table A.7).

Affective rating Behavioral analysis is based on 41 subjects ($n_{\text{LTM}} = 22, n_{\text{MNP}} = 19$)², of which 34 did not miss any rating, 5 missed 1, and 2 missed 3 ratings. Mean mood rating during the scan across all subjects and conditions was 100.80, which represents an overall neutral to slightly positive mood on our Self-Assessment Mannikins scale.

In the linear mixed effect model, condition significantly predicted affect. Compared to SC ($b = 46.74, \text{CI} [15.75, 78.26]$), all conditions lead to a significantly higher affective rating (NT $b = 84.91, \text{CI} [53.64, 119.03]$, NNSC $b = 107.05, \text{CI} [75.04, 139.09]$, SP $b = 139.69, \text{CI} [107.14, 170.99]$), confirming our experimental manipulation (see Figure 5.6). Group did not significantly predict overall affective ratings ($b = 21.02, \text{CI} [-14.93, 70.76]$). But the interaction between group and condition was positive for SP and NNSC compared to SC stimuli, indicating that the difference in affective ratings between self-related positive compared to self-related negative adjectives was significantly smaller in LTM compared to MNP (SP $b = -32.44, \text{CI} [-52.85, -11.75]$). As NNSC were experienced significantly less negative than SC, it could not serve as a negative, non-self referential control condition for SC and was not further analyzed on the neural level.

²A technical problem with the track ball lead to a high amount of missing responses in three cases (19, 15 and 10 out of 24).

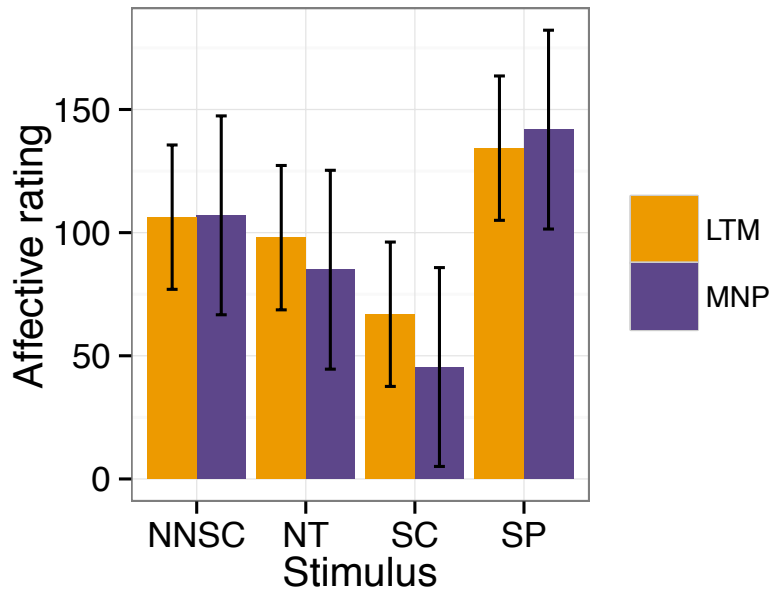


Figure 5.6: Affective ratings after each condition for meditators (LTM, orange) and meditation-naïve participants (MNP, purple). Bars indicate fixed effects estimates of the linear mixed model for each stimulus type within each group. Error bars depict 95% confidence intervals. NNSC negative not self-critical, NT neutral, SC self-critical, SP self-praising.

FMRI results Subjects with more than 1.5 mm of head movement in one direction were excluded from fMRI analysis, resulting in analyzed 41 subjects (Table 5.4), which did not differ from our full sample in sociodemographics or matching. FMRI results showed the same regions when adding an additional regressor to control for gender (results not shown).

Table 5.4: Sociodemographic variables of subjects included in fMRI analysis.

	MNP ($n = 21$)		LTM ($n = 20$)		Statistic (df)	p
	M	SD	M	SD		
Age	44.76	10.70	47	11.11	$t(39) = -.56$.58
Gender (f/m)	11/10		12/8		$\chi^2(1) = .03$.86
Education (years)	18.24	3.74	19.05	4.50	$t(39) = -.66$.51
IQ (MWT-B)	123.33	13.32	118.18	13.19	$t(39) = 1.21$.23

Abbreviations MWT-B Mehrfachwahl-Wortschatz-Intelligenz-Test

Self-relevant versus neutral stimuli $SC > NT$ led to increased activations in mid-frontal regions, the insula, precuneus and visual areas in both groups (Figure 5.7). At the group level, we found significantly higher activation in the DMPFC region (superior frontal/paracingulate, BA 8; 8744 mm³) for LTM compared to MNP.

The contrast $SP > NT$ resulted in similar but larger and stronger activations compared to $SC > NT$ in both groups (Figure 5.7). In the group comparison, LTM again showed significantly more activation in the DMPFC during $SP > NT$ (BA 6, 17400 mm³). Additionally, we found increased activation for LTM compared to MNP in widespread clusters, covering left middle-frontal, bilateral inferior prefrontal and insular areas, basal ganglia, visual areas including the fusiform gyrus, and mid-brain, thalamus, and adjacent left hippocampal/amygdalar regions.

The conjunction analysis of SC and SP stimuli versus NT resulted in a significant group difference in the DMPFC area (Table 5.5).

Note that middle-frontal, mid-brain, and hippocampal/amygdalar regions were significantly activated in LTM in the $SP > NT$ and $SC > NT$, while we found no such activations for MNP. While this difference survived the corrected group comparison only in the $SP > NT$ contrast, it hints at a quantitative rather than qualitative difference in these regions between $SC > NT$ and $SP > NT$ for the group comparison (Figure 5.7).

Table 5.5: Brain activations related to the main effect of group: LTM>MNP

Brain regions		BA	Coordinates			<i>z</i>	<i>p</i>	
			<i>x</i>	<i>y</i>	<i>z</i>			
<i>SC >NT</i>								
Superior Frontal/Paracingulate	M (DMPFC)	8	-4	34	52	4.09	< .01	**
<i>SP >NT</i>								
Superior Frontal/Paracingulate	M (DMPFC)	6	6	16	48	4.28	< .0001	†
Middle Frontal	L	6	-34	6	48	3.50		
Frontal Pole	R	10	32	58	-2	4.11	< .0001	†
Inferior Frontal	R	44	48	18	10	3.38		
Inferior Frontal	L	44/45	-52	36	-6	3.74		
Insula	R	13	34	22	0	3.67		
Insula	L	13	-28	20	0	3.92		
Putamen	R		48	18	10	3.32		
Putamen	L		-24	10	0	3.66		
Occipital Lobe/Precuneus/Cuneus	M	18/31	-10	-74	28	3.73	< .01	**
Temporo-occipital Lobe/Fusiform	L	19	-24	-56	-4	4.22	< .0001	†
Temporo-occipital Lobe/Fusiform	R	19	28	-48	-6	4.15		
Brainstem/Medulla			-4	-36	-42	3.97		
Cerebellum/Pyramis			-26	-42	-42	3.89		
<i>Conjunction SC >NT AND SP >NT</i>								
Superior Frontal/Paracingulate	M (DMPFC)	6	6	16	48	3.97	.03	*

Clusterwise corrected with $p = .05$ (FWE) at whole-brain level.

Significance levels: * $p < .05$, ** $p < .01$, *** $p < .001$, † $p < .0001$

Abbreviations LTM mid-to-long-term meditators, MNP meditation-naive participants, BA Brodmann area, DMPFC dorso-medial prefrontal cortex, R right, L left, M medial

One indentation: absolute cluster maxima, two indentations: local clustermaxima.

Stereotaxic coordinates are based on the human atlas of MNI, BA are based on Talairach Daemon labels in FSL view.

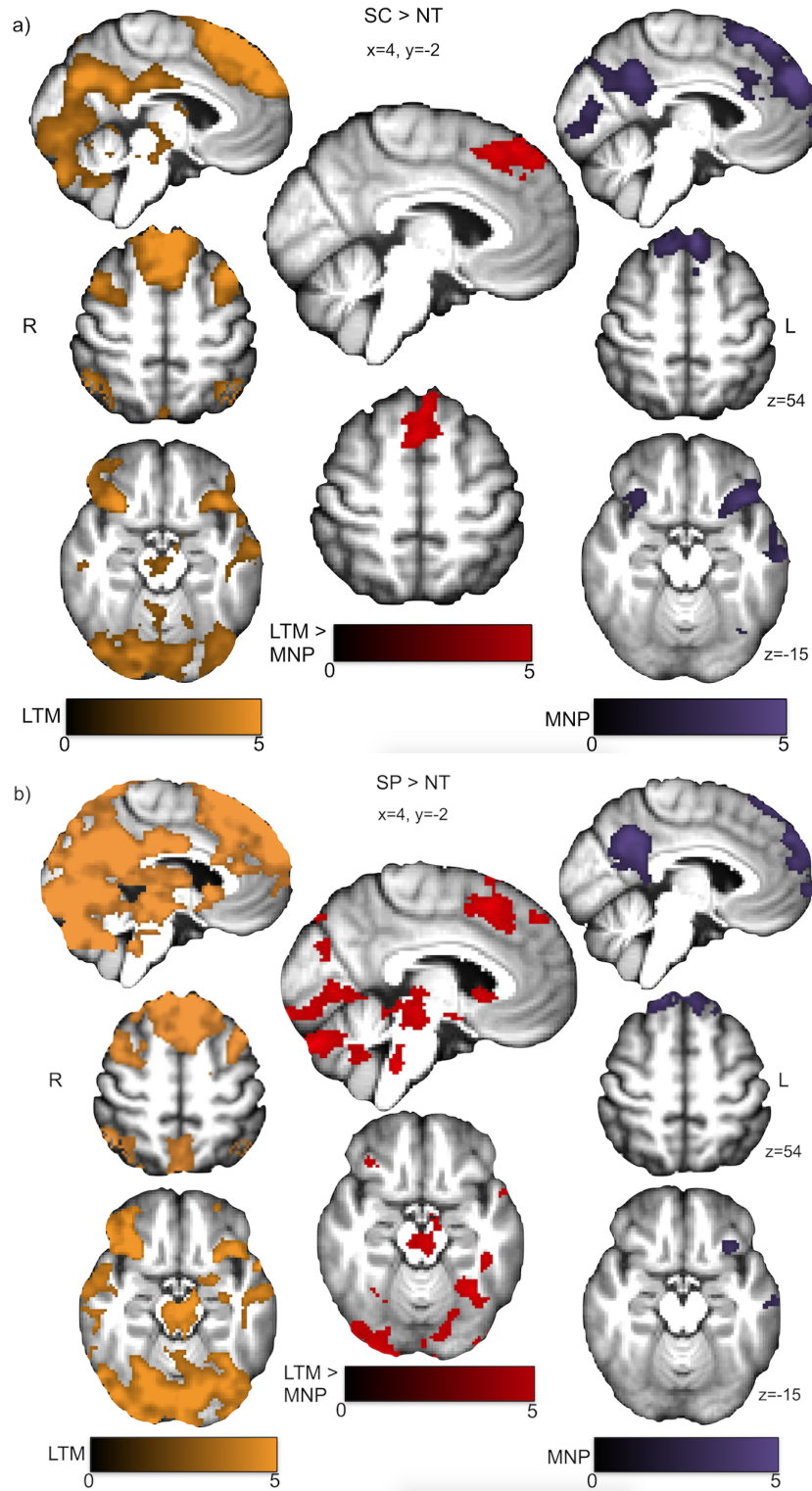


Figure 5.7: Neural activations of a) self-critical versus neutral (SC>NT) and b) self-positive versus neutral (SP>NT) stimuli. Probability maps depict significant results for meditators (LTM, orange), meditation-naive participants (MNP, purple) and the group comparison LTM>MNP (red).

Correlation results Correlation analysis between mean activation of the DMPFC cluster resulting from the conjunction analysis (see Appendix C, Figure C.2) and the FFMQ factors *observe* and *non-react* revealed significant correlations with non-react. For SP > NT it was $r(39) = .32, p = .04$. Examining the individual groups, we found that the correlation was driven by LTM ($r(19) = .49, p = .03$), while there was no significant association in MNP ($r(20) = -.18, p = .44$). The difference between the regression slopes after a Fisher-r-z transformation was significant ($z=2.10, p=.04$) (Figure 5.8 a). For SC > NT, we found a significant correlation for both groups together ($r(39) = .34, p = .03$) and a trend for LTM ($r(19) = .39, p = .09$), while MNP showed no correlation ($r(20) = -.09, p = .70$) (Figure 5.8 b). However, the correlation coefficients did not differ significantly between groups ($z = 1.49, p = .14$). DMPFC activation was not related to hours of meditation training or practice intensity ($p > .20$).

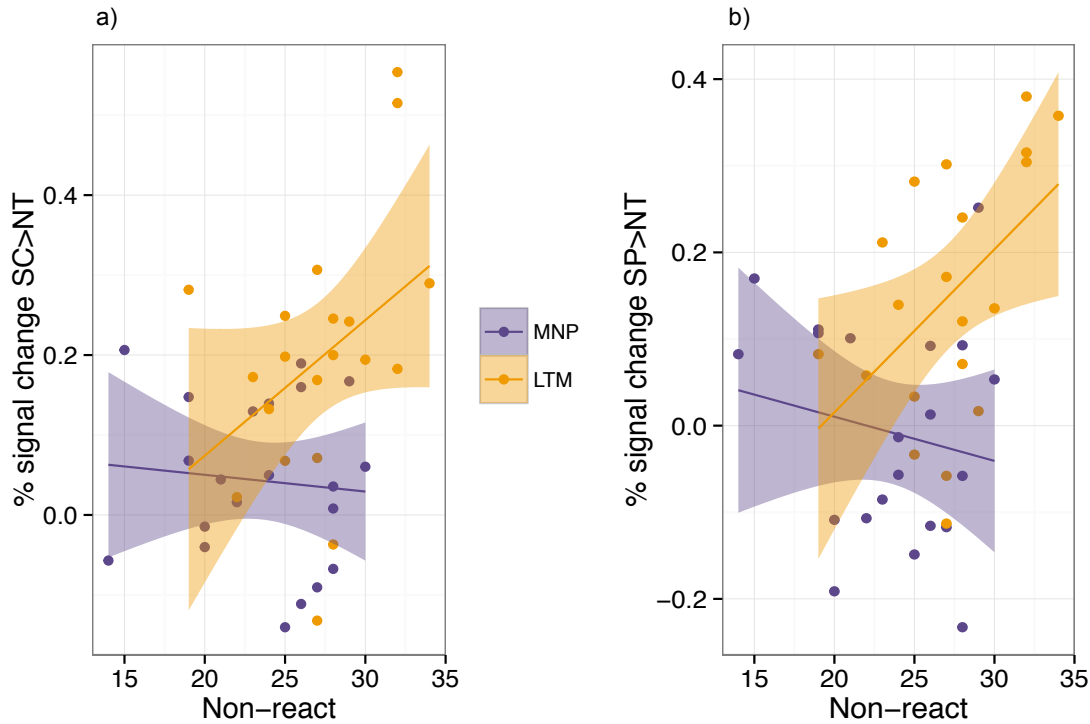


Figure 5.8: Correlations between mean % signal change of the DMPFC conjunction cluster with FFMQ non-react scores during a) self-critical versus neutral (SC>NT) and b) self-praising versus neutral (SP>NT).

Psycho-physiological interaction For LTM, we did not find a significant difference in the linear relation (PPI effect) between the DMPFC and another region in the brain during self-related emotional conditions (EMO) compared to NT. For MNP, we found a positive PPI effect for EMO compared to NT, in regions comprising the precuneus area extending into occipital/superior parietal regions (left and right), and a cluster in the left temporal gyrus. In the group comparison MNP>LTM, we found similar regions,

namely clusters in the precuneus/occipital areas (see Figure 5.9), indicating that MNP showed stronger functional connectivity with these regions during EMO compared to NT conditions (for a schematic representation see Appendix C, Figure C.3).

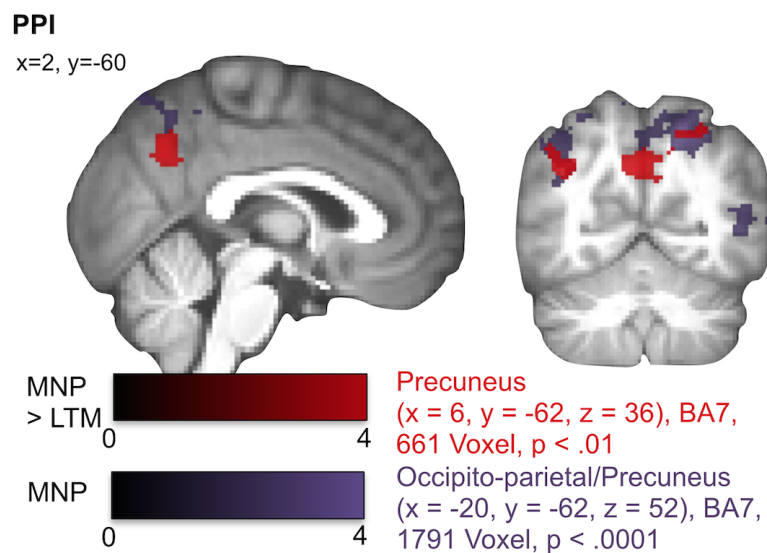


Figure 5.9: Functional connectivity difference between emotional self-related (EMO) and neutral (NT) stimuli for MNP (purple) and for the group comparison MNP>LTM (red). Areas in the precuneus and occipito-parietal regions were found in both analyses. Cluster coordinates of peak activation, region (including Brodmann area), cluster size, and peak significance are indicated.

Discussion

This study investigated trait differences in behavioral and neural correlates of individualized positive and negative self-appraisals between mindfulness meditators and meditation-naïve participants, during a non-meditation task. We hypothesized habitual differences between these groups when confronted with self-referential emotional stimuli, more specifically a decreased emotional reactivity to such stimuli in meditators. Indeed, we found less extreme affective ratings after self-appraisals in this group. On the neural level, they showed more pronounced activation during self-appraisals in frontal and limbic regions, particularly during positive self-appraisal. Further, their DMPFC activation correlated with a non-reacting attitude towards inner experience and was less functionally connected with posterior mid-line and parietal regions.

Questionnaire and behavioral results To our surprise, the groups showed only few differences in measures of mindfulness and related constructs. One reason could be the limited comparability of self-report mindfulness questionnaires between meditators and non-meditators (Grossman and Van Dam, 2011; Van Dam et al., 2009) despite matched samples (Baer, 2011). Our groups differed in the factor *non-react*, reflecting a difference in general emotion regulation, i.e. allowing inner experiences and feelings to come and go (Hölzel et al., 2011). Non-react has been found to predict general well-being, decreased psychological symptoms (Baer et al., 2006), and increases with mindfulness training (Baer et al., 2008). For self-compassion we only found a group difference in the total score at trend level, and only if not corrected for multiple-comparisons. Again, this is somewhat surprising, given the reported relations between mindfulness and self-compassion (Hollis-Walker and Colosimo, 2011). One reason might be that open monitoring techniques have no particular focus on self-compassion (Lutz et al., 2007). Thus, other factors such as life-style or working in the field of mental health might influence the level of self-compassion similarly or more (Baer et al., 2008). Overall, the fact that the groups did not differ more regarding the questionnaires might also reflect a strength of the current study. We ensured a good matching of LTM with a healthy control group, consisting of equally high-functioning individuals, with on average good education, high levels of intelligence, and a comparable percentage working in mental health related areas. Thus, group differences we do find in our study are arguably also be less influenced by selection bias and demand characteristics, which are potential confounds in cross-sectional studies with meditators (Davidson, 2010).

Affective ratings We found group differences in affective ratings after blocks of SP compared to SC, suggesting that the difference between positive experience after SP and negative experience after SC was less pronounced for LTM. This pattern is in line with

the notion of increased emotional balance as a result of mindfulness training. When faced with self-appraisals, LTM potentially appraised them in a more detached, non-reactive way, identifying less strongly with these stimuli (Hölzel et al., 2011). This interpretation is corroborated by the fact that we did not find a difference in affective ratings after NT blocks and that the number of chosen adjectives and their evaluation before the scan was the same for the two groups. However, we can not fully rule out demand characteristics, since LTM are probably aware of the assumed relation between emotional reactivity and mindfulness training. At the same time, meditators might be more aware of their affective state and better able to describe their affects (Fox et al., 2012; Sze et al., 2010). The tendency of lower TAS scores in our LTM sample points into the same direction. Thus, differences in affective ratings between groups must be interpreted with caution.

FMRI Results In general SC and SP showed similar activation patterns, in both groups. Brühl et al. (2014) also reported similar activation during self-criticism and self-praise, corroborating the notion that different emotional experiences share similar brain regions (Lindquist et al., 2012). Group differences were hypothesized in emotion processing, self-referential and regulative prefrontal areas.

Differences in emotion-generative structures during self-criticism and self-praise Unlike the previous study by Doerig et al. (2014), we observed no consistent amygdala activation during SC. On this basis, our hypothesis regarding group-differences in this region can not be answered completely. However, LTM showed activation bordering the left hippocampus/amygdala region for SC >NT and a similar activation during SP >NT, while we found no such pattern for MNP. Only the latter was significantly different in the group comparison. For these regions, we propose a quantitative threshold effect rather than a qualitative difference, and interpret that LTM show evidence for stronger emotional processing of both self-referential conditions compared to NT. We found a similar pattern for visual cortex activations, which could reflect less cognitive avoidance (Servaas et al., 2014), again suggesting stronger emotional processing in LTM. These findings might reflect higher present-moment awareness and acceptance of emotions in this group, which is partly in line with the finding of decreased control over emotion generative structures during emotional stimulation in experienced meditators (Taylor et al., 2011). However, it contradicts previous findings of decreased activation in emotion-generative structures in meditators (Brefczynski-Lewis et al., 2007; Chiesa et al., 2013). For SP >NT, there was additional evidence for increased emotional processing in LTM compared to MNP. LTM showed increased activation in the ventromedial orbitofrontal cortex/ventral striatum, which could indicate higher reward and subjective pleasantness of positive self-appraisals (Kühn and Gallinat, 2012; McClure et al., 2004). Further, the insula, another key region for emotion generation and experience, showed increased

activation in LTM, which could signify stronger emotional arousal resulting from less regulation and more acceptance of emotional states (Grant et al., 2011), or higher emotional awareness and monitoring of internal states during self-related emotions (Craig, 2004; Lutz et al., 2008).

Overall, neural activations in emotion generative structures seemed increased for both valences in LTM, contradicting our behavioral results. A possible explanation is the timing of stimulation and rating: LTM might have been more accepting and aware of their immediate affective reaction during SP and SC blocks instead of regulating their experience. Such a non-reactive attitude could result in increased emotional processing *during* emotional stimulation, similar to findings by (Taylor et al., 2011), while affective ratings *after* the actual experience might be less extreme.

Differential activation in regulative prefrontal and mid-line structures

Similar to previous studies by Doerig et al. (2014) and Brühl et al. (2014) we found activations in anterior and posterior cortical midline structures associated with self-referential and autobiographical memory processing and default mode self-reference (Fossati et al., 2014; Johnson, 2002; Northoff et al., 2006; Whitfield-Gabrieli et al., 2011).

Interestingly, these mid-line activations were more pronounced in LTM in both contrasts. This is consistent with previous research: Creswell et al. (2007) found that higher dispositional mindfulness was associated with increased DMPFC activation in an affect labeling task, and Hölzel et al. (2007) found DMPFC activation in a similar sample of meditators during meditation compared to arithmetics and suggested increased processing of emotions, like being aware of, identifying and attending to one's emotions (Phan et al., 2004). This is in line with the common functional interpretation of the dorsal MPFC as the cognitive/appraising part of emotion processing (Etkin et al., 2011; Schmitz and Johnson, 2006), and could therefore represent a key region for improved emotion regulation abilities related to mindfulness training (Hölzel et al., 2007). In fact, differential activation in the DMPFC has also been reported in relation to emotion regulation, in studies on reappraisal of negative pictures (Ochsner et al., 2002; Ochsner and Gross, 2005). However, studies also report decreased MPFC activation in meditators during emotional processing in a mindful state (Brefczynski-Lewis et al., 2007; Grant et al., 2011; Taylor et al., 2011), and less mid-line, default mode activation in during resting state (Brewer et al., 2011). Differences in meditation experience might partly explain these inconsistencies. Deactivations are particularly reported for very experienced meditators (Brefczynski-Lewis et al., 2007; Chiesa et al., 2013). As we found no correlation with meditation experience in this region we can not add further evidence for this hypothesis. Other reasons for the contradictory results might lie in the specific task (e.g. active self-reference) and location of mid-line activation (dorsal versus ventral).

In our experiment, the positive relation between DMPFC activation and the factor *non-react* supports the interpretation of the DMPFC activation as a functional correlate of

cognitive, appraising processes (Etkin et al., 2011), which in the case of LTM might illustrate an accepting and non-reactive appraisal of inner experience. The fact that the correlations seemed mostly driven by LTM, at least for SP, might indicate a behavioral shift in the reaction towards positive self-appraisals, which might be distinctive for meditation practitioners.

Similar to the DMPFC, LTM showed increased activations in lateral mid- and inferior prefrontal regions during SC and SP versus NT, with the latter surviving the group comparison. Apart from the interpretation as a typical emotion regulation area (Ochsner et al., 2002; Ochsner and Gross, 2005; Phillips et al., 2003), mindfulness-related interpretations have been suggested for lateral prefrontal areas, such as cognitive labeling of emotional stimuli (Hariri et al., 2003; Taylor et al., 2003), focused attention and open awareness (Manna et al., 2010), or the ability to observe thoughts and emotions in a detached manner (Fox et al., 2014).

Taken together, differential activations in frontal regions could reflect stronger self-awareness and focus on inner feelings, and “mindful emotion regulation” in the sense of a non-reactive attitude towards these experiences in LTM.

Differential functional connectivity during SP and SC between groups

We found positive functional coupling between the DMPFC and regions in the precuneus and occipito-parietal lobe for self-relevant emotional conditions compared to neutral words in MNP. Functional coupling in these regions was also significantly stronger in MNP compared to LTM. In LTM, emotional self-related stimuli did not result in differential functional connectivity between the DMPFC and other regions.

The precuneus is part of the default mode network and has been implicated in general autobiographical memory retrieval and self-processing (Cavanna and Trimble, 2006; Northoff et al., 2006), while the adjacent occipito-parietal areas are relevant for visual attention (Pessoa et al., 2002). The stronger, positive functional coupling between midline regions in MNP might reflect stronger self-focus or attentional processing when facing emotional self-referential words compared to neutral words, while attention and/or self-focus seemed less influenced by stimulus type in LTM. A similar interpretation, namely reduced self-focused attention in meditators, was put forward by Garrison et al. (2014), who found reduced functional connectivity in the precuneus/PCC in meditators during loving kindness meditation. However, these interpretations remain tentative and should ideally be corroborated with behavioral measures on the degree of self-focused processing.

Limitations and future directions Our interpretations of brain activations in meditators remain speculative, as our findings are only partially in line with previous studies in meditators and the interpretations draw from assumptions based on traditional claims that meditators approach emotional self-appraisals in “healthier” ways. At the same time, our cross-sectional design, can not exclude that meditators are drawn to practices

like meditation because they are more interested or in need of developing skills to deal with emotions. Similarly, they might differ in other relevant personality or life-style factors from MNP. Further, as mentioned earlier, we can not exclude demand characteristics. Even though we feel it is important to study concepts of self-praise and self-criticism in experienced meditators, our results should be verified in longitudinal designs, especially as we found no significant association between the amount of meditation training and activation in the DMPFC. Regarding our samples, both groups were healthy and rather high-functioning in terms of intelligence, highest degree and occupation. It will therefore be important to expand upon our results by conducting similar experiments in more diverse and clinical samples.

With introducing the self-praise condition, we probably lost the ability to study harsh self-criticism, as we did not observe stable amygdala activation during self-criticism. At the same time we found the biggest activations and group differences during SP. Thus we gained new insights into possible links between positive affect and mindfulness - a relationship we are only beginning to study and which needs further research. Such research should incorporate concepts of positive psychology such as resilience, positive outlook on life, and well-being, to fully grasp the potential of mindfulness training in the clinical setting.

We observed differences in an active self-referential task. Still, group differences might be associated with underlying difference in the resting state. Future studies should ideally combine self-referential and resting state analysis to shed light on the relation between these two modes of self-processing.

Lastly, with our design we can not fully disentangle emotional from self-referential aspects, since the neutral stimuli differed from self-criticism and self-praise in valence as well as in self-reference. From a theoretical perspective, it would be difficult to fully disentangle these two dimensions: On the one hand descriptions of aspect of the self are in most cases emotionally colored. On the other hand emotional stimuli per definition are salient to the individual and involve self-related processes. Future studies might employ factorial designs to try and disentangle the influence of these two dimensions.

Chapter 6

Discussion

6.1 Main findings

This thesis started out by asking how mindfulness training influences habitual ways of self-related processing. To answer this question, two studies compared mid-to-long-term mindfulness meditators (LTM) with matched meditation-naïve participants (MNP) regarding different aspects of self-related processes using functional magnetic imaging (fMRI).

The first study investigated short periods of mindful self-awareness (FEEL), and compared them to periods of cognitive self-reference (THINK). Increased activation in somatosensory regions associated with body awareness and decreased activation in cognitive self-referential cortical mid-line structures (CMS) were hypothesized, particularly in LTM.

During FEEL versus THINK, both groups displayed increased activations in somatosensory regions and decreased activations in frontal and posterior CMS. Decreases were significantly larger in LTM regarding the dorso-medial prefrontal cortex (DMPFC), and LTM showed reduced activations in the left inferior-lateral prefrontal cortex. Further, only LTM showed increased activation in the bilateral insula and reductions in the amygdala. However, there was no significant group difference regarding these regions. MNP reported higher verbalizing of their experience during the FEEL condition compared to LTM.

In the second study we investigated behavioral and neural correlates of individualized self-praising (SP) and self-critical (SC) stimuli (compared to neutral stimuli). Less extreme affective ratings in LTM and lower activations in emotion-generative structures were hypothesized. Further, differences in top-down and self-referential structures were explored, also regarding their functional connectivity with other regions.

When comparing affective ratings after SP and SC, LTM showed a smaller difference between these conditions compared to MNP. On the neural level, group comparisons revealed stronger activations in emotion-generative regions in LTM during self-appraisals compared to neutral stimuli. LTM further displayed stronger DMPFC activations. Both differences were particularly prominent during SP. Activation in the DMPFC correlated with a non-reacting attitude towards inner experience, as assessed by the Five Facets Mindfulness Questionnaire (FFMQ). Further, the DMPFC activation in LTM showed no difference in functional connectivity to other regions when comparing self-appraisals

with neutral stimuli. The same analysis in MNP revealed increased connectivity between DMPFC and posterior CMS and parietal regions.

6.2 Integration

Mindful self-awareness, as studied in the first experiment, is not only related to the experiential self (Gallagher, 2000), but is also similar to a mode of self-awareness, which is trained in mindfulness meditation. This mode is characterized by an intentional focus on momentary experiences such as body sensations or feelings. Accordingly, Hölzel et al. (2011)’s framework proposed an increase in body awareness in meditators, related to activations in somatosensory areas. In our study, when comparing FEEL to THINK, increased bilateral somatosensory activations were found in both groups. The extent of these activations seemed larger in LTM, but the direct group comparison showed no significant difference. These findings strengthen the notion that attention to body sensation and feelings is a capability that is already present in untrained individuals, as demonstrated in previous studies (Bauer et al., 2014; Herwig et al., 2010), but might develop further with training.

Another proposed effect of meditation is a change in the perspective on the self (Hölzel et al., 2011). For example, it has been argued that increased awareness on present-moment sensations and feelings reduces cognitive self-reference and rumination (Farb et al., 2013; Vago and Silbersweig, 2012). This shift is probably related to functional changes in prefrontal and posterior CMS (Brewer et al., 2011; Farb et al., 2007). In our experiment, both groups displayed decreased activations in prefrontal and posterior CMS during mindful self-awareness. However, decreases in the prefrontal CMS were significantly stronger in LTM, indicating that this group reduced cognitive self-reference stronger than MNP. The difference was in the DMPFC rather than more anterior CMS, consistent with the group differences reported by Farb et al. (2007). The DMPFC has been associated with evaluative functions (Northoff and Bermpohl, 2004). This could mean that meditation-naïve participants had a higher tendency to evaluate self-related phenomena compared to meditators.

Further, LTM showed reduced activation in the left inferior-lateral prefrontal cortex including the language and inner-speech related Brocca’s area (Morin and Michaud, 2007), which was significantly different from MNP. As such, LTM probably relied less on verbal labeling of experience during FEEL, while it might have been a strategy in untrained individuals to remain with momentary experiences (Lieberman et al., 2007; Torrisi et al., 2013). This interpretation is in line with higher reported verbalizing during FEEL in MNP (as assessed in a structured interview after the scan). It is surprising that no deactivation in the inferior-lateral prefrontal cortex was observed in meditators by Farb et al. (2007). Farb et al. (2007)’s study was similar to our paradigm, but used trait adjectives. The

6.2. INTEGRATION

lack of language related stimuli in our paradigm might have been particularly suited to detect differences between groups regarding spontaneous labeling of experience during mindful awareness.

Finally, we found decreased amygdala activations during FEEL versus THINK in LTM only, but groups did not differ significantly in this area. Amygdala decrease during mindful awareness has been reported for meditation-naïve participants by Herwig et al. (2010), but only for meditators by Farb et al. (2007). Our results provide some evidence that LTM showed decreased emotional reactivity to sensations and feelings. The lack of a group difference could mean that at least in this experiment on different modes of self-processing without emotional stimuli, other factors might influence amygdala results, such as the nature of the control task.

Decreased emotional reactivity in LTM was however explicitly hypothesized in our second study on self-appraisals, more explicitly towards self-criticism (SC) and self-praise (SP). LTM showed less extreme affective ratings after these blocks compared to MNP, which was in line with this hypothesis. On the neural level though, LTM showed stronger activations in emotion-generative structures during self-appraisals, particularly during SP. This result stands in contrast to the hypothesis of decreased emotion related activations during meditation (Brefczynski-Lewis et al., 2007). However, a study by Taylor et al. (2011) reported no reduction in the amygdala during negative emotional pictures and an increase during positive pictures in meditators. The fact that positive self-appraisals show the biggest group differences is remarkable. Meditation training should decrease the seeking for and attachment to positive emotions and might even reduce SP-associated *positive* affect (Lalot et al., 2014). On the other hand, mindfulness has been related to increased positive emotions and self-esteem. To address this apparent discrepancy, we note that the instruction in our experiment to process SP and their meaning, is probably less related to actively seeking self-praise, but to openly perceiving their emotional valence and meaning. And LTM might have processed these emotions more strongly without trying to change them (Chambers et al., 2009). Another explanation could be that our findings reflect a slightly westernized form of mindfulness, where happiness, wellbeing and self-enhancement might constitute additional goals besides weakening self-attachment (Hollis-Walker and Colosimo, 2011).

Regarding the DMPFC, most studies suggest decreases in this region in meditators corresponding to decreased cognitive self-processing (Brewer et al., 2011; Farb et al., 2007) or decreased evaluation of emotions (Grant et al., 2011; Taylor et al., 2011). However, some mindfulness-related studies have reported increases in this region. Hölzel et al. (2007) reported higher activation in meditators during focused attention on the breath and interpreted it as increased emotional processing. Emotion regulation studies in meditation-naïve subjects found that higher DMPFC activation was associated with higher trait mindfulness and successful reappraisal (Modinos et al., 2010; Lutz et al.,

2014). Our paradigm contained aspects of emotion processing and self-reference, and in the above studies the DMPFC has been associated with both processes. This complicates reaching a conclusion about the activation in our experiment, especially since we know of no pertinent fMRI research into self-related emotions in meditators. A possible indication provides the correlation between DMPFC activation and the non-reacting facet of the FFMQ. It suggests that mindfulness meditators might have employed a form of “mindful reappraisal”, in the sense that they would process SC and SP more strongly without trying to react to them or change them. It is however possible that meditators with even more expertise would show decreased CMS activations comparable to previous findings (Brefczynski-Lewis et al., 2007; Grant et al., 2011), indicative of reduced reappraisal of any form.

Interpretations of the differences in functional connectivity between the DMPFC and other brain regions, when comparing self-appraisals with neutral words, must remain similarly tentative. The positive functional coupling between mid-line regions in MNP could reflect stronger self-focus or attentional processing of SC and SP while LTM showed no such differential coupling related to self-appraisals. In fact, reduced functional connectivity in the posterior CMS has been reported in meditators during loving kindness, and was interpreted reduced self-focused attention by Garrison et al. (2014).

The results of the two presented studies complement the current knowledge on self-related processes in several interesting ways. For the first time, different self-related processes were studied in the same sample of meditators, thereby opening the possibility to draw overarching conclusions on changes in the self, related to mindfulness training. Further, we presented the first study, which used individualized self-critical and self-praising stimuli in mindfulness meditators, who aspire a balanced attitude towards such stimuli. This type of study has important clinical health indications as extreme self-focus and self-related emotions (e.g. self-criticism) can lead to mental health related disorders like depression. The alteration from significantly decreased DMPFC activations during mindful self-awareness to significantly increased activations during self-appraisal, challenges the notion of consistently reduced CMS activations in LTM compared to MNP. In particular, the increased DMPFC activations during self-appraisals could reflect that LTM were more ready and open to attentively process these emotional stimuli.

From the clinical perspective, the first study corroborated previous notions of a quieting of cognitive self-reference during mindful awareness, which seemed fostered in mindfulness meditators. The second study indicated a more balanced emotional experience during self-appraisals based on affective ratings. And activations in the DMPFC and emotion-related structures could present a mindful emotion regulation strategy during SC and SP in this group.

Overall, states of mindful self-awareness appeared more accessible for untrained individuals, while a more balanced relation towards self-appraisals might require more training.

6.3 Limitations

The cross-sectional design of the studies limits the conclusions we can draw from our results with respect to meditation training in general. As Davidson (2010) and others point out, long-term training in meditation might only be undertaken by a particular group of individuals who already had different interests and characteristics and ultimately different brains before they started meditation training. Typically, cross-sectional studies attempt to overcome these limitations by correlating the amount of meditation experience with the extent of the observed changes (Brefczynski-Lewis et al., 2007). However, in this work we found no such association. We believe that the very diverse mindfulness experience in our sample of meditators prevented us from detecting developmental trajectories of mindfulness practice (Christopher et al., 2012). Nevertheless, our results provide an important first step on the way to uncovering possible changes in self-related processes as a result of mindfulness training.

Another caveat is that pertinent research is scarce and some of our interpretations are built on traditional assumptions that mindfulness training leads to healthier minds. However, we lack behavioral measures, for example about the extent of self-focus or attachment to the self, to corroborate these interpretations. Thus, it remains crucial to verify these traditional assumptions in future meditation studies.

6.4 Outlook

The studies presented in this thesis are first steps towards a better understanding of mindfulness-related changes in self-functions and their neural underpinnings. Future steps should corroborate and extend these findings in additional studies on meditators, and in studies on clinical populations who follow mindfulness-based therapies.

Ideally, efforts should combine cross-sectional and longitudinal approaches, and complement neuroscientific data with relevant behavioral measures, such as affective ratings applied here. Longitudinal investigations of meditation-training induced habitual changes pose many practical difficulties, as these changes occur over longer time-scales. Cross-sectional studies should therefore remain a valuable means to provide insights into altered self-related processes and emotion regulation in meditators. Given the relevance of such changes for meditation practitioners and therapeutical applications, it is surprising how little mindfulness studies try to assess changes beyond the meditative state. Thus, more cross-sectional studies should look into habitual changes in meditators and employ similarly naturalistic designs as utilized here, to maximize the conclusions we can draw for

every-day mental health related functions. Finally, such studies should also try to measure behavioral correlates of these processes, for example the extent of self-focus, to build a solid ground for interpreting neuroscientific findings.

Another interesting avenue would be to study certain sub-components of mindfulness independently. For example, we could try to specify how body awareness alone is related to emotion regulation on the neural level, and then identify whether, and how, mindfulness training transcends these effects. A possible way to accomplish this is to study professionals (e.g. dancers) who require body awareness and attention on the body and compare them to meditators and matched control groups (compare Sze et al., 2010).

The growing integration of mobile technology into our daily lives could partially mitigate the discussed problems involved with longitudinal studies on expert meditators. Online-dairies could track meditation training, and some behavioral experiments could be administered online. For a subset of participants additional neuroscientific measures could be acquired (see Heller et al., 2015 for a similar approach). Such studies would permit to compare larger samples regarding factors such as different training protocols, personality, or cultural background, and synthesize how these relate to changes in self-processing and emotion regulation.

To learn more about the therapeutical potential of mindfulness training for healthier self-related processes, longitudinal studies are essential. In this context, it will be important to disentangle specific mindfulness-related effects from unspecific factors. For such inferences, active control groups are needed (see for example Rosenkranz et al., 2013). Longitudinal studies in large clinical samples further hold the promise of identifying neural or behavioral predictors regarding treatment success. This could be used, for instance, to identify which form of mindfulness practice is most suited and approachable for a given patient (Simon and Engström, 2015). In view of the many different forms of mindfulness training and potentially relevant personal, cultural and biological factors which could influence training success, we need large samples to establish such links. To this end, we could again envision mobile applications to acquire data from participants in mindfulness programs and measure neural correlates in a subset of participants.

Even though we found limited differences in affective ratings between our groups, further attempts should also be made to bridging the gap between objective data and subjective experience (Cacioppo and Decety, 2011). Thus, future work should integrate the subjective experience during meditation training, during experimental manipulations and in everyday situations, for example in the form of “experience samples”. Integrating subjective reports can advance our understanding of this introspective practice per se, as illustrated in a study by Hasenkamp et al. (2012). In addition, subjects’ experiences during meditation and their perception of meditation might influence their perseverance and “training success”.

6.5 Conclusion

This thesis presented results from two fMRI studies on habitual self-related processes in experienced mindfulness meditators. We found a central role for prefrontal mid-line regions in this group. Their activation was reduced during experiential self-awareness compared to self-reference, reminiscent of a quieting of self-related thinking and evaluation. When presented with self-criticism and self-praise, however, the activation in this region was increased. This higher activation during self-appraisals might reflect a mindful attitude to face such stimuli in an accepting and non-reactive way. The findings and their discussion expand on current knowledge of possible mechanisms through which mindfulness training could influence self-related functions, and ultimately mental health.

Bibliography

- Andersson, J. L. R., Jenkinson, M., and Smith, S. (2007). Non-linear registration aka spatial normalisation. Technical Report FMRIB technical report TR07JA2, FMRIB Analysis Group of the University of Oxford.
- Angleitner, A., Ostendorf, F., and John, O. P. (1990). Towards a taxonomy of personality descriptors in German: a psycholexical study. *European Journal of Personality*, 4(2):89–118.
- Annett, M. (1970). A classification of hand preference by association analysis. *British Journal of Psychology*, 61(3):303–321.
- Bach, M., Bach, D., de Zwaan, M., Serim, M., and Böhmer, F. (1996). Validation of the German version of the 20-item Toronto Alexithymia Scale in normal persons and psychiatric patients. *Psychotherapie, Psychosomatik, Medizinische Psychologie*, 46(1):23–28.
- Baer, R. A. (2003). Mindfulness training as a clinical intervention: a conceptual and empirical review. *Clinical Psychology: Science and Practice*, 10(2):125–143.
- Baer, R. A. (2009). Self-focused attention and mechanisms of change in mindfulness-based treatment. *Cognitive Behaviour Therapy*, 38(S1):15–20.
- Baer, R. A. (2011). Measuring mindfulness. *Contemporary Buddhism*, 12(1):241–261.
- Baer, R. A., Smith, G. T., Hopkins, J., Krietemeyer, J., and Toney, L. (2006). Using self-report assessment methods to explore facets of mindfulness. *Assessment*, 13(1):27–45.
- Baer, R. A., Smith, G. T., Lykins, E., Button, D., Krietemeyer, J., Sauer, S., Walsh, E., Duggan, D., and Williams, J. M. G. (2008). Construct validity of the Five Facet Mindfulness Questionnaire in meditating and nonmeditating samples. *Assessment*, 15(3):329–342.
- Bates, D., Maechler, M., Bolker, B., and Walker, S. (2014). lme4: Linear mixed-effects models using Eigen and S4. Technical report, R package version 1.1-7.
- Bauer, C. C. C., Barrios, F. A., and Díaz, J. L. (2014). Subjective somatosensory experiences disclosed by focused attention: cortical-hippocampal-insular and amygdala contributions. *PLoS One*, 9(8):e104721–e104721.

- Beckmann, C. F., Jenkinson, M., and Smith, S. M. (2003). General multilevel linear modeling for group analysis in fMRI. *Neuroimage*, 20(2):1052–1063.
- Bezzola, L., Mérillat, S., and Jäncke, L. (2012). Motor training-induced neuroplasticity. *GeroPsych: The Journal of Gerontopsychology and Geriatric Psychiatry*, 25(4):189–197.
- Bishop, S. R., Lau, M., Shapiro, S., Carlson, L., Anderson, N. D., Carmody, J., Segal, Z. V., Abbey, S., Speca, M., Velting, D., and Devins, G. (2004). Mindfulness: a proposed operational definition. *Clinical Psychology: Science and Practice*, 11(3):230–241.
- Blanke, O. and Mohr, C. (2005). Out-of-body experience, heautoscopy, and autoscopic hallucination of neurological origin. Implications for neurocognitive mechanisms of corporeal awareness and self-consciousness. *Brain Research Reviews*, 50(1):184–199.
- Bliese, P. (2013). *multilevel, R package version 2.5*.
- Bonnelle, V., Ham, T. E., Leech, R., Kinnunen, K. M., Mehta, M. A., Greenwood, R. J., and Sharp, D. J. (2012). Salience network integrity predicts default mode network function after traumatic brain injury. *Proceedings of the National Academy of Sciences*, 109(12):4690–4695.
- Boubela, R. N., Kalcher, K., Huf, W., Seidel, E.-M., Derntl, B., Pezawas, L., Nasel, C., and Moser, E. (2015). fMRI measurements of amygdala activation are confounded by stimulus correlated signal fluctuation in nearby veins draining distant brain regions. *Scientific Reports*, 5.
- Bradley, M. M. and Lang, P. J. (1994). Measuring emotion: the self-assessment manikin and the semantic differential. *Journal of Behavior Therapy and Experimental Psychiatry*, 25(1):49–59.
- Brefczynski-Lewis, J. A., Lutz, A., Schaefer, H. S., Levinson, D. B., and Davidson, R. J. (2007). Neural correlates of attentional expertise in long-term meditation practitioners. *Proceedings of the National Academy of Sciences*, 104(27):11483–11488.
- Brewer, J. A., Garrison, K. A., and Whitfield-Gabrieli, S. (2013). What about the "self" is processed in the posterior cingulate cortex? *Frontiers in Human Neuroscience*, 7.
- Brewer, J. A., Worhunsky, P. D., Gray, J. R., Tang, Y. Y., Weber, J., and Kober, H. (2011). Meditation experience is associated with differences in default mode network activity and connectivity. *Proceedings of the National Academy of Sciences*, 108(50):20254–20259.
- Brown, K. W., Ryan, R. M., and Creswell, J. D. (2007). Mindfulness: theoretical foundations and evidence for its salutary effects. *Psychological Inquiry*, 18(4):211–237.

BIBLIOGRAPHY

- Brühl, A. B., Rufer, M., Kaffenberger, T., Baur, V., and Herwig, U. (2014). Neural circuits associated with positive and negative self-appraisal. *Neuroscience*, 265:48–59.
- Cacioppo, J. T. and Decety, J. (2011). Social neuroscience: challenges and opportunities in the study of complex behavior. *Annals of the New York Academy of Sciences*, 1224(1):162–173.
- Cahn, B. R. and Polich, J. (2006). Meditation states and traits: EEG, ERP, and neuroimaging studies. *Psychological Bulletin*, 132(2):180–211.
- Callard, F. and Margulies, D. S. (2014). What we talk about when we talk about the default mode network. *Frontiers in Human Neuroscience*, 8:619.
- Cavanna, A. E. and Trimble, M. R. (2006). The precuneus: a review of its functional anatomy and behavioural correlates. *Brain*, 129(3):564–583.
- Chambers, R., Gullone, E., and Allen, N. B. (2009). Mindful emotion regulation: an integrative review. *Clinical Psychology Review*, 29(6):560–572.
- Chambers, R., Lo, B. C. Y., and Allen, N. B. (2007). The impact of intensive mindfulness training on attentional control, cognitive style, and affect. *Cognitive Therapy and Research*, 32(3):303–322.
- Chiesa, A. (2012). The difficulty of defining mindfulness: current thought and critical issues. *Mindfulness*, 4(3):255–268.
- Chiesa, A. and Malinowski, P. (2011). Mindfulness-based approaches: are they all the same? *Journal of Clinical Psychology*, 67(4):404–424.
- Chiesa, A. and Serretti, A. (2010). A systematic review of neurobiological and clinical features of mindfulness meditations. *Psychological Medicine*, 40(08):1239–1252.
- Chiesa, A., Serretti, A., and Jakobsen, J. C. (2013). Mindfulness: top-down or bottom-up emotion regulation strategy? *Clinical Psychology Review*, 33(1):82–96.
- Christopher, M. S., Charoensuk, S., Gilbert, B. D., Neary, T. J., and Pearce, K. L. (2009). Mindfulness in Thailand and the United States: a case of apples versus oranges? *Journal of Clinical Psychology*, 65(6):590–612.
- Christopher, M. S., Neuser, N. J., Michael, P. G., and Baitmangalkar, A. (2012). Exploring the psychometric properties of the Five Facet Mindfulness Questionnaire. *Mindfulness*, 3(2):124–131.
- Cisler, J. M., Bush, K., and Steele, J. S. (2014). A comparison of statistical methods for detecting context-modulated functional connectivity in fMRI. *Neuroimage*, 84:1042–1052.

- Craig, A. D. (2003). Interoception: the sense of the physiological condition of the body. *Current Opinion in Neurobiology*, 13(4):500–505.
- Craig, A. D. (2004). Human feelings: why are some more aware than others? *Trends in Cognitive Sciences*, 8(6):239–241.
- Creswell, J. D., Way, B. M., Eisenberger, N. I., and Lieberman, M. D. (2007). Neural correlates of dispositional mindfulness during affect labeling. *Psychosomatic Medicine*, 69(6):560–565.
- Critchley, H. D., Wiens, S., Rotshtein, P., Ohman, A., and Dolan, R. J. (2004). Neural systems supporting interoceptive awareness. *Nature Neuroscience*, 7(2):189–195.
- Damasio, A. R. (2000). *The feeling of what happens: body, emotion and the making of consciousness*. Harcourt Brace, New York.
- Davidson, R. J. (2010). Empirical explorations of mindfulness: conceptual and methodological conundrums. *Emotion*, 10(1):8–11.
- Davidson, R. J. and Lutz, A. (2008). Buddha’s brain: neuroplasticity and meditation. *IEEE Signal Processing Magazine*, 25(1):176.
- Davis, D. M. and Hayes, J. A. (2011). What are the benefits of mindfulness? A practice review of psychotherapy-related research. *Psychotherapy*, 48(2):198–208.
- Disner, S. G., Beevers, C. G., Haigh, E. A. P., and Beck, A. T. (2011). Neural mechanisms of the cognitive model of depression. *Nature Reviews Neuroscience*, 12(8):467–477.
- Doerig, N., Schlumpf, Y., Spinelli, S., Späti, J., Brakowski, J., Quednow, B. B., Seifritz, E., and Grosse Holtforth, M. (2014). Neural representation and clinically relevant moderators of individualised self-criticism in healthy subjects. *Social Cognitive and Affective Neuroscience*, 9(9):1333–1340.
- Eberth, J. and Sedlmeier, P. (2012). The effects of mindfulness meditation: a meta-analysis. *Mindfulness*, 3(3):174–189.
- Etkin, A., Egner, T., and Kalisch, R. (2011). Emotional processing in anterior cingulate and medial prefrontal cortex. *Trends in Cognitive Sciences*, 15(2):85–93.
- Farb, N. A. S., Segal, Z. V., and Anderson, A. K. (2013). Mindfulness meditation training alters cortical representations of interoceptive attention. *Social Cognitive and Affective Neuroscience*, 8(1):15–26.
- Farb, N. A. S., Segal, Z. V., Mayberg, H., Bean, J., McKeon, D., Fatima, Z., and Anderson, A. K. (2007). Attending to the present: mindfulness meditation reveals distinct neural modes of self-reference. *Social Cognitive and Affective Neuroscience*, 2(4):313–322.

BIBLIOGRAPHY

- Fossati, P., Hevenor, S. J., Graham, S. J., Grady, C., Keightley, M. L., Craik, F., and Mayberg, H. (2014). In search of the emotional self: an fMRI study using positive and negative emotional words. *American Journal of Psychiatry*, 160(11):1938–1945.
- Fox, K. C. R., Nijeboer, S., Dixon, M. L., Floman, J. L., Ellamil, M., Rumak, S. P., Sedlmeier, P., and Christoff, K. (2014). Is meditation associated with altered brain structure? A systematic review and meta-analysis of morphometric neuroimaging in meditation practitioners. *Neuroscience and Biobehavioral Reviews*, 43:48–73.
- Fox, K. C. R., Zakarauskas, P., Dixon, M., Ellamil, M., Thompson, E., and Christoff, K. (2012). Meditation experience predicts introspective accuracy. *PLoS One*, 7(9):e45370.
- Friston, K. J. (1994). Functional and effective connectivity in neuroimaging: a synthesis. *Human Brain Mapping*, 2(1-2):56–78.
- Friston, K. J., Buechel, C., Fink, G. R., Morris, J., Rolls, E., and Dolan, R. J. (1997). Psychophysiological and modulatory interactions in neuroimaging. *Neuroimage*, 6(3):218–229.
- Fulton, P. R. (2010). Anatta: self, non-self, and the therapist. In Hick, S. F. and Bien, T., editors, *Mindfulness and the Therapeutic Relationship*, chapter 4, pages 55–71. The Guilford Press, New York.
- Gallagher, S. (2000). Philosophical conceptions of the self: implications for cognitive science. *Trends in Cognitive Sciences*, 4(1):14–21.
- Garrison, K. A., Scheinost, D., Constable, R. T., and Brewer, J. A. (2014). BOLD signal and functional connectivity associated with loving kindness meditation. *Brain and Behavior*, 4(3):337–347.
- Goyal, M., Singh, S., Sibinga, E. M. S., Gould, N. F., Rowland-Seymour, A., Sharma, R., Berger, Z., Sleicher, D., Maron, D. D., Shihab, H. M., Ranasinghe, P. D., Linn, S., Saha, S., Bass, E. B., and Haythornthwaite, J. A. (2014). Meditation programs for psychological stress and well-being: a systematic review and meta-analysis. *JAMA Internal Medicine*, 174(3):357–368.
- Grant, J. A., Courtemanche, J., and Rainville, P. (2011). A non-elaborative mental stance and decoupling of executive and pain-related cortices predicts low pain sensitivity in Zen meditators. *Pain*, 152(1):150–156.
- Greenberg, J. and Pyszczynski, T. (1986). Persistent high self-focus after failure and low self-focus after success: the depressive self-focusing style. *Journal of Personality and Social Psychology*, 50(5):1039–1044.

- Greve, D. N. and Fischl, B. (2009). Accurate and robust brain image alignment using boundary-based registration. *Neuroimage*, 48(1):63–72.
- Gross, J. J. and Muñoz, R. F. (1995). Emotion regulation and mental health. *Clinical Psychology: Science and Practice*, 2(2):151–164.
- Gross, J. J. and Thompson, R. A. (2007). *Handbook of emotion regulation: Conceptual foundations*. Guilford Publications, New York.
- Grossman, P. (2011). Defining mindfulness by how poorly I think I pay attention during everyday awareness and other intractable problems for psychology’s (re)invention of mindfulness: Comment on Brown et al. (2011). *Psychological Assessment*, 23(4):1034–1040.
- Grossman, P. and Van Dam, N. T. (2011). Mindfulness, by any other name...: trials and tribulations of sati in western psychology and science. *Contemporary Buddhism*, 12(1):219–239.
- Gu, J., Strauss, C., Bond, R., and Cavanagh, K. (2015). How do mindfulness-based cognitive therapy and mindfulness-based stress reduction improve mental health and wellbeing? A systematic review and meta-analysis of mediation studies. *Clinical Psychology Review*, 37:1–12.
- Gusnard, D. A., Akbudak, E., Shulman, G. L., and Raichle, M. E. (2001). Medial prefrontal cortex and self-referential mental activity: relation to a default mode of brain function. *Proceedings of the National Academy of Sciences*, 98(7):4259–4264.
- Hamilton, J. P., Furman, D. J., Chang, C., Thomason, M. E., Dennis, E., and Gotlib, I. H. (2011). Default-mode and task-positive network activity in major depressive disorder: implications for adaptive and maladaptive rumination. *Biological Psychiatry*, 70(4):327–333.
- Hariri, A. R., Mattay, V. S., Tessitore, A., Fera, F., and Weinberger, D. R. (2003). Neocortical modulation of the amygdala response to fearful stimuli. *Biological Psychiatry*, 53(6):494–501.
- Hart, R., Ivtzan, I., and Hart, D. (2013). Mind the gap in mindfulness research: a comparative account of the leading schools of thought. *Review of General Psychology*, 17(4):453–466.
- Hasenkamp, W., Wilson-Mendenhall, C. D., Duncan, E., and Barsalou, L. W. (2012). Mind wandering and attention during focused meditation: a fine-grained temporal analysis of fluctuating cognitive states. *Neuroimage*, 59(1):750–760.

BIBLIOGRAPHY

- Heller, A. S., Fox, A. S., Wing, E. K., McQuisition, K. M., Vack, N. J., and Davidson, R. J. (2015). The neurodynamics of affect in the laboratory predicts persistence of real-world emotional responses. *The Journal of Neuroscience*, 35(29):10503–10509.
- Herwig, U., Kaffenberger, T., Jäncke, L., and Brühl, A. B. (2010). Self-related awareness and emotion regulation. *Neuroimage*, 50(2):734–741.
- Hollis-Walker, L. and Colosimo, K. (2011). Mindfulness, self-compassion, and happiness in non-meditators: a theoretical and empirical examination. *Personality and Individual Differences*, 50(2):222–227.
- Hölzel, B. K., Carmody, J., Evans, K. C., Hoge, E. A., Dusek, J. A., Morgan, L., Pitman, R. K., and Lazar, S. W. (2009). Stress reduction correlates with structural changes in the amygdala. *Social Cognitive and Affective Neuroscience*, 5(1):11–17.
- Hölzel, B. K., Lazar, S. W., Gard, T., Schuman-Olivier, Z., Vago, D. R., and Ott, U. (2011). How does mindfulness meditation work? Proposing mechanisms of action from a conceptual and neural perspective. *Perspectives on Psychological Science*, 6(6):537–559.
- Hölzel, B. K., Ott, U., Hempel, H., Hackl, A., Wolf, K., Stark, R., and Vaitl, D. (2007). Differential engagement of anterior cingulate and adjacent medial frontal cortex in adept meditators and non-meditators. *Neuroscience Letters*, 421(1):16–21.
- Hupfeld, J. and Ruffieux, N. (2011). Validierung einer deutschen Version der Self-Compassion Scale (SCS-D). *Zeitschrift für Klinische Psychologie und Psychotherapie*, 40(2):115–123.
- Ionta, S., Martuzzi, R., Salomon, R., and Blanke, O. (2014). The brain network reflecting bodily self-consciousness: a functional connectivity study. *Social Cognitive and Affective Neuroscience*, 9(12):1904–1913.
- Jain, S., Shapiro, S. L., Swanick, S., Roesch, S. C., Mills, P. J., Bell, I., and Schwartz, G. E. R. (2007). A randomized controlled trial of mindfulness meditation versus relaxation training: effects on distress, positive states of mind, rumination, and distraction. *Annals of Behavioral Medicine*, 33(1):11–21.
- James, W. (1890). *Principles of psychology*. Henry-Holt and co, New York, 1 edition.
- Jäncke, L. (2013). *Lehrbuch Kognitive Neurowissenschaften*. Verlag Hans Huber, Bern.
- Jang, J. H., Jung, W. H., Kang, D. H., Byun, M. S., Kwon, S. J., Choi, C. H., and Kwon, J. S. (2011). Increased default mode network connectivity associated with meditation. *Neuroscience Letters*, 487(3):358–362.

- Jenkinson, M., Bannister, P., Brady, M., and Smith, S. (2002). Improved optimization for the robust and accurate linear registration and motion correction of brain images. *Neuroimage*, 17(2):825–841.
- Jenkinson, M. and Smith, S. (2001). A global optimisation method for robust affine registration of brain images. *Medical Image Analysis*, 5(2):143–156.
- Johnson, S. C. (2002). Neural correlates of self-reflection. *Brain*, 125(8):1808–1814.
- Joormann, J. and Gotlib, I. H. (2010). Emotion regulation in depression: relation to cognitive inhibition. *Cognition and Emotion*, 24(2):281–298.
- Kabat-Zinn, J. (1990). *Full catastrophe living: the programm of the Stress Reduction Clinic at the Universität of Massachusetts Medical Center*. Delta, New York.
- Kabat-Zinn, J. (1994). *Wherever you go, there you are: mindfulness meditation in everyday life*. Hyperion.
- Kabat-Zinn, J. (2003). Mindfulness-based interventions in context: past, present, and future. *Clinical Psychology: Science and Practice*, 10(2):144–156.
- Keng, S. L., Smoski, M. J., and Robins, C. J. (2011). Effects of mindfulness on psychological health: a review of empirical studies. *Clinical Psychology Review*, 31(6):1041–1056.
- Kerr, C. E., Josyula, K., and Littenberg, R. (2011). Developing an observing attitude: an analysis of meditation diaries in an MBSR clinical trial. *Clinical Psychology and Psychotherapy*, 18(1):80–93.
- Khalsa, S. S., Rudrauf, D., Damasio, A. R., Davidson, R. J., Lutz, A., and Tranel, D. (2008). Interoceptive awareness in experienced meditators. *Psychophysiology*, 45(4):671–677.
- Khoury, B., Lecomte, T., Fortin, G., Masse, M., Therien, P., Bouchard, V., Chapleau, M.-A., Paquin, K., and Hofmann, S. G. (2013). Mindfulness-based therapy: a comprehensive meta-analysis. *Clinical Psychology Review*, 33(6):763–771.
- Kiken, L. G., Garland, E. L., Bluth, K., Palsson, O. S., and Gaylord, S. A. (2015). From a state to a trait: trajectories of state mindfulness in meditation during intervention predict changes in trait mindfulness. *Personality and Individual Differences*, 81:41–46.
- Killingsworth, M. A. and Gilbert, D. T. (2010). A wandering mind is an unhappy mind. *Science*, 330(6006):932–932.
- Krohne, H. W., Egloff, B., and Kohlmann, C. W. (1996). Untersuchungen mit einer deutschen Version der 'Positive and Negative Affect Schedule' (PANAS). *Diagnostica*, 42(2):139–156.

BIBLIOGRAPHY

- Kühn, S. and Gallinat, J. (2012). The neural correlates of subjective pleasantness. *Neuroimage*, 61(1):289–294.
- Laird, A. R., Robinson, J. L., McMillan, K. M., Tordesillas-Gutiérrez, D., Moran, S. T., Gonzales, S. M., Ray, K. L., Franklin, C., Glahn, D. C., Fox, P. T., and Lancaster, J. L. (2010). Comparison of the disparity between Talairach and MNI coordinates in functional neuroimaging data: validation of the Lancaster transform. *Neuroimage*, 51(2):677–683.
- Lalot, F., Delplanque, S., and Sander, D. (2014). Mindful regulation of positive emotions: a comparison with reappraisal and expressive suppression. *Frontiers in Psychology*, 5:243.
- Langer, E. J. and Moldoveanu, M. (2000). The construct of mindfulness. *Journal of Social Issues*, 56(1):1–9.
- Lehrl, S. (1977). *Mehrfachwahl-Wortschatz-Intelligenztest MWT-B*. Spitta, Balingen, 5 edition.
- Lemogne, C., Delaveau, P., Freton, M., Guionnet, S., and Fossati, P. (2012). Medial prefrontal cortex and the self in major depression. *Journal of Affective Disorders*, 136(1):e1–e11.
- Lieberman, M. D. and Cunningham, W. A. (2009). Type I and Type II error concerns in fMRI research: re-balancing the scale. *Social Cognitive and Affective Neuroscience*, 4(4):423–428.
- Lieberman, M. D., Eisenberger, N. I., Crockett, M. J., Tom, S. M., Pfeifer, J. H., and Way, B. M. (2007). Putting feelings into words: affect labeling disrupts amygdala activity in response to affective stimuli. *Psychological Science*, 18(5):421–428.
- Lindquist, K. A., Wager, T. D., Kober, H., Bliss-Moreau, E., and Barrett, L. F. (2012). The brain basis of emotion: a meta-analytic review. *Behavioral and Brain Sciences*, 35(3):121–143.
- Linehan, M. M. (1994). Acceptance and change: the central dialectic in psychotherapy. In Hayes S. C., Jacobson N. S., Follette V M., D. M. J., editor, *Acceptance and Change: Content and Context Psychotherapy*, pages 73–90. Context Press, Reno.
- Lipp, I., Murphy, K., Wise, R. G., and Caseras, X. (2014). Understanding the contribution of neural and physiological signal variation to the low repeatability of emotion-induced BOLD responses. *Neuroimage*, 86:335–342.
- Logothetis, N. K. (2008). What we can do and what we cannot do with fMRI. *Nature*, 453(7197):869–878.

- Logothetis, N. K., Pauls, J., Augath, M., Trinath, T., and Oeltermann, A. (2001). Neurophysiological investigation of the basis of the fMRI signal. *Nature*, 412(6843):150–157.
- Luders, E., Toga, A. W., Lepore, N., and Gaser, C. (2009). The underlying anatomical correlates of long-term meditation: larger hippocampal and frontal volumes of gray matter. *Neuroimage*, 45(3):672–678.
- Lutz, A., Dunne, J. D., and Davidson, R. J. (2007). Meditation and the neuroscience of consciousness: an introduction. In Zelazo, P., Moscovitch, M., and Thompson, E., editors, *Cambridge Handbook of Consciousness*. Cambridge University Press.
- Lutz, A., Greischar, L. L., Perlman, D. M., and Davidson, R. J. (2009). BOLD signal in insula is differentially related to cardiac function during compassion meditation in experts vs. novices. *Neuroimage*, 47(3):1038–1046.
- Lutz, A., Slagter, H. A., Dunne, J. D., and Davidson, R. J. (2008). Attention regulation and monitoring in meditation. *Trends in Cognitive Sciences*, 12(4):163–169.
- Lutz, J., Brühl, A. B., Dörig, N., Scheerer, H., Achermann, R., Weibel, A., Jäncke, L., and Herwig, U. (2016). Altered processing of self-related emotional stimuli in mindfulness meditators. *Neuroimage*, 124:958–967.
- Lutz, J., Herwig, U., Opialla, S., Hittmeyer, A., Jäncke, L., Rufer, M., Holtforth, M. G., and Brühl, A. B. (2014). Mindfulness and emotion regulation – an fMRI study. *Social Cognitive and Affective Neuroscience*, 9(6):776–785.
- Manna, A., Raffone, A., Perrucci, M. G., Nardo, D., Ferretti, A., Tartaro, A., Londei, A., Del Gratta, C., Belardinelli, M. O., and Romani, G. L. (2010). Neural correlates of focused attention and cognitive monitoring in meditation. *Brain Research Bulletin*, 82(1-2):46–56.
- McClure, S. M., York, M. K., and Montague, P. R. (2004). The neural substrates of reward processing in humans: the modern role of FMRI. *The Neuroscientist*, 10(3):260–268.
- Michalak, J., Heidenreich, T., Ströhle, G., and Nachtigall, C. (2008). Die deutsche Version der Mindful Attention and Awareness Scale (MAAS). Psychometrische Befunde zu einem Achtsamkeitsfragebogen. *Zeitschrift für Klinische Psychologie und Psychotherapie*, 37(3):200–208.
- Mikulas, W. L. (2007). Buddhism & western psychology: fundamentals of integration. *Journal of Consciousness Studies*, 14(4):4–49.

BIBLIOGRAPHY

- Modinos, G., Ormel, J., and Aleman, A. (2010). Individual differences in dispositional mindfulness and brain activity involved in reappraisal of emotion. *Social Cognitive and Affective Neuroscience*, 5(4):369–377.
- Mor, N. and Winkquist, J. (2002). Self-focused attention and negative affect: a meta-analysis. *Psychological Bulletin*, 128(4):638–662.
- Morin, A. and Michaud, J. (2007). Self-awareness and the left inferior frontal gyrus: inner speech use during self-related processing. *Brain Research Bulletin*, 74(6):387–396.
- Mumford, J. (2007). A guide to calculating percent change with featquery – unpubl. tech rep. http://mumford.fmripower.org/perchange_guide.pdf, accessed: 2014-07-01.
- Nachev, P., Wydell, H., O’neill, K., Husain, M., and Kennard, C. (2007). The role of the pre-supplementary motor area in the control of action. *Neuroimage*, 36:T155–T163.
- Neff, K. (2003). Self-compassion: an alternative conceptualization of a healthy attitude toward oneself. *Self and Identity*, 2(2):85–101.
- Neisser, U. (1988). Five kinds of self-knowledge. *Philosophical Psychology*, 1(1):35–59.
- Nichols, T., Brett, M., Andersson, J., Wager, T., and Poline, J. B. (2005). Valid conjunction inference with the minimum statistic. *Neuroimage*, 25(3):653–660.
- Nolen-Hoeksema, S., Wisco, B. E., and Lyubomirsky, S. (2008). Rethinking rumination. *Perspectives on Psychological Science*, 3(5):400–424.
- Northoff, G. (2007). Psychopathology and pathophysiology of the self in depression - neuropsychiatric hypothesis. *Journal of Affective Disorders*, 104(1):1–14.
- Northoff, G. and Bermpohl, F. (2004). Cortical midline structures and the self. *Trends in Cognitive Sciences*, 8(3):102–107.
- Northoff, G., Heinzel, A., de Greck, M., Bermpohl, F., Dobrowolny, H., and Panksepp, J. (2006). Self-referential processing in our brain - a meta-analysis of imaging studies on the self. *Neuroimage*, 31(1):440–457.
- Ochsner, K. N., Bunge, S. A., Gross, J. J., and Gabrieli, J. D. E. (2002). Rethinking feelings: an fMRI study of the cognitive regulation of emotion. *Journal of Cognitive Neuroscience*, 14(8):1215–1229.
- Ochsner, K. N. and Gross, J. J. (2005). The cognitive control of emotion. *Trends in Cognitive Sciences*, 9(5):242–249.

- O'Reilly, J. X., Woolrich, M. W., Behrens, T. E. J., Smith, S. M., and Johansen-Berg, H. (2012). Tools of the trade: psychophysiological interactions and functional connectivity. *Social Cognitive and Affective Neuroscience*, 7(5):604–609.
- Pali Text Society (1921). The Pali text society's Pali–English dictionary.
- Pessoa, L., Kastner, S., and Ungerleider, L. G. (2002). Attentional control of the processing of neutral and emotional stimuli. *Cognitive Brain Research*, 15(1):31–45.
- Phan, K. L., Taylor, S. F., Welsh, R. C., Decker, L. R., Noll, D. C., Nichols, T. E., Britton, J. C., and Liberzon, I. (2003). Activation of the medial prefrontal cortex and extended amygdala by individual ratings of emotional arousal: a fMRI study. *Biological Psychiatry*, 53(3):211–215.
- Phan, K. L., Wager, T. D., Taylor, S. F., and Liberzon, I. (2004). Functional neuroimaging studies of human emotions. *CNS Spectrums*, 9(4):258–266.
- Phillips, M. L., Drevets, W. C., Rauch, S. L., and Lane, R. (2003). Neurobiology of emotion perception I: the neural basis of normal emotion perception. *Biological Psychiatry*, 54(5):504–514.
- Poline, J. B. and Brett, M. (2012). The general linear model and fMRI: does love last forever? *Neuroimage*, 62(2):871–880.
- Pruessmann, K. P., Weiger, M., Scheidegger, M. B., and Boesiger, P. (1999). SENSE: sensitivity encoding for fast MRI. *Magnetic Resonance in Medicine*, 42(5):952–962.
- Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., and Shulman, G. L. (2001). A default mode of brain function. *Proceedings of the National Academy of Sciences*, 98(2):676–682.
- Rosenkranz, M. A., Davidson, R. J., Maccoon, D. G., Sheridan, J. F., Kalin, N. H., and Lutz, A. (2013). A comparison of mindfulness-based stress reduction and an active control in modulation of neurogenic inflammation. *Brain, Behavior, and Immunity*, 27(1):174–184.
- RStudio (2012). RStudio: integrated development environment for R (Version 0.98.953).
- Schmitz, T. W. and Johnson, S. C. (2006). Self-appraisal decisions evoke dissociated dorsal-ventral aMPFC networks. *Neuroimage*, 30(3):1050–1058.
- Servaas, M. N., Riese, H., Ormel, J., and Aleman, A. (2014). The neural correlates of worry in association with individual differences in neuroticism. *Human Brain Mapping*, 35(9):4303–4315.

BIBLIOGRAPHY

- Shapiro, S. L., Carlson, L. E., Astin, J. A., and Freedman, B. (2006). Mechanisms of mindfulness. *Journal of Clinical Psychology*, 62(3):373–386.
- Sherry, S. B., Mackinnon, S. P., Macneil, M. A., and Fitzpatrick, S. (2012). Discrepancies confer vulnerability to depressive symptoms: a three-wave longitudinal study. *Journal of Counseling Psychology*, 60(1):112–126.
- Silananda, U. and Heinze, R. I. (1995). *The four foundations of mindfulness*. Simon und Schuster.
- Simon, R. and Engström, M. (2015). The default mode network as a biomarker for monitoring the therapeutic effects of meditation. *Frontiers in Psychology*, 6:776.
- Smith, S. M. (2002). Fast robust automated brain extraction. *Human Brain Mapping*, 17(3):143–155.
- Smith, S. M., Jenkinson, M., Woolrich, M. W., Beckmann, C. F., Behrens, T. E. J., Johansen-Berg, H., Bannister, P. R., De Luca, M., Drobnjak, I., Flitney, D. E., Niazy, R. K., Saunders, J., Vickers, J., Zhang, Y., De Stefano, N., Brady, J. M., and Matthews, P. M. (2004). Advances in functional and structural MR image analysis and implementation as FSL. *Neuroimage*, 23(S1):208–219.
- Ströhle, G., Nachtigall, C., Michalak, J., and Heidenreich, T. (2010). Measuring mindfulness as a multidimensional construct: a German version of the Kentucky Inventory of Mindfulness Skills (KIMS-D). *Zeitschrift für Klinische Psychologie, Psychiatrie und Psychotherapie*, 39(1):1–12.
- Sze, J. a., Gyurak, A., Yuan, J. W., and Levenson, R. W. (2010). Coherence between emotional experience and physiology: does body awareness training have an impact? *Emotion*, 10(6):803–814.
- Tang, Y. Y., Hölzel, B. K., and Posner, M. I. (2015). The neuroscience of mindfulness meditation. *Nature Reviews Neuroscience*, 16(4):213–225.
- Taylor, G. J., Ryan, D., and Bagby, R. M. (1985). Toward the development of a new self-report alexithymia scale. *Psychotherapy and Psychosomatics*, 44(4):191–199.
- Taylor, S. F., Phan, K., Decker, L. R., and Liberzon, I. (2003). Subjective rating of emotionally salient stimuli modulates neural activity. *Neuroimage*, 18(3):650–659.
- Taylor, V. A., Grant, J., Daneault, V., Scavone, G., Breton, E., Roffe-Vidal, S., Courtemanche, J., Lavarenne, A. S., and Beauregard, M. (2011). Impact of mindfulness on the neural responses to emotional pictures in experienced and beginner meditators. *Neuroimage*, 57(4):1524–1533.

- Thompson, B. L. and Waltz, J. A. (2008). Mindfulness, self-esteem, and unconditional self-acceptance. *Journal of Rational-Emotive and Cognitive-Behavior Therapy*, 26(2):119–126.
- Torrisi, S. J., Lieberman, M. D., Bookheimer, S. Y., and Altshuler, L. L. (2013). Advancing understanding of affect labeling with dynamic causal modeling. *Neuroimage*, 82:481–488.
- Vago, D. R. and Silbersweig, D. A. (2012). Self-awareness, self-regulation, and self-transcendence (S-ART): a framework for understanding the neurobiological mechanisms of mindfulness. *Frontiers in Human Neuroscience*, 6:296–296.
- Van Dam, N. T., Earleywine, M., and Danoff-Burg, S. (2009). Differential item function across meditators and non-meditators on the Five Facet Mindfulness Questionnaire. *Personality and Individual Differences*, 47(5):516–521.
- Watson, D., Clark, L. A., and Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect. *Journal of Personality and Social Psychology*, 54(6):1063–1070.
- Way, B. M., Creswell, J. D., Eisenberger, N. I., and Lieberman, M. D. (2010). Dispositional mindfulness and depressive symptomatology: correlations with limbic and self-referential neural activity during rest. *Emotion*, 10(1):12–24.
- Whitfield-Gabrieli, S. and Ford, J. M. (2012). Default mode network activity and connectivity in psychopathology. *Annual Review of Clinical Psychology*, 8:49–76.
- Whitfield-Gabrieli, S., Moran, J. M., Nieto-Castañón, A., Triantafyllou, C., Saxe, R., and Gabrieli, J. D. E. (2011). Associations and dissociations between default and self-reference networks in the human brain. *Neuroimage*, 55(1):225–232.
- Wickham, H. (2009). *ggplot2: elegant graphics for data analysis*. Springer New York.
- Woolrich, M. W. (2008). Robust group analysis using outlier inference. *Neuroimage*, 41(2):286–301.
- Woolrich, M. W., Behrens, T. E. J., Beckmann, C. F., Jenkinson, M., and Smith, S. M. (2004). Multilevel linear modelling for fMRI group analysis using Bayesian inference. *Neuroimage*, 21(4):1732–1747.
- Woolrich, M. W., Ripley, B. D., Brady, M., and Smith, S. M. (2001). Temporal autocorrelation in univariate linear modeling of fMRI data. *Neuroimage*, 14(6):1370–1386.
- World Medical Association (1992). Declaration of Geneva.
- Worsley, K. J. (2001). Statistical analysis of activation images. *Functional MRI: An Introduction to Methods*, 14:251–270.

BIBLIOGRAPHY

- Zeidan, F. (2015). The neurobiology of mindfulness meditation. In Brown, K. W., Creswell, J. D., and Ryan, R. M., editors, *The Handbook of Mindfulness*, pages 171–189. The Guilford Press, New York, 1 edition.
- Zung, W. W. (1965). A self-rating depression scale. *Archives of General Psychiatry*, 12(1):63–70.
- Zung, W. W. (2005). Self-rating depression scale. In *Collegium Internationale Psychiatricae Sclalarum, Internationale Skalen für Psychiatrie*, volume 12, pages 63–70. Beltz, Göttingen.

Appendix A

Sample characteristics

Meditation experience

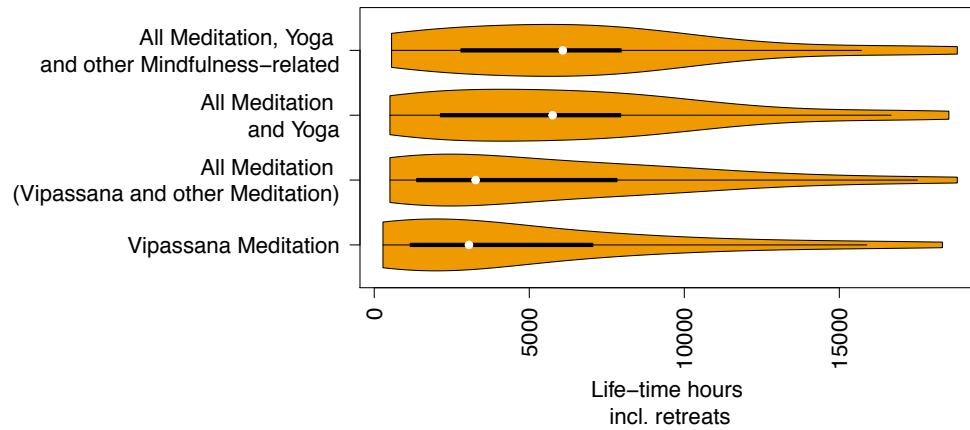


Figure A.1: Violinplot (box plot combined with kernel density plot) depicting median and distribution of meditators' meditation and mindfulness-related experience. Other mindfulness-related include Qi-Gong, Tai Chi, Kung Fu.

Table A.1:

Description of meditators' meditation and mindfulness-related experience (life-time hours, incl. retreats) ($n = 22$)

Variable	M	SD	min	max
Vipassana Meditation	4861.50	4999.74	281	18325
All Meditation (Vipassana, other Meditation)	5970.91	5505.93	506	18805
All Meditation, Yoga	6759.82	5442.43	506	18533
All Meditation, Yoga, other Mindfulness-related	7011.25	5337.95	558	18805

Current practice

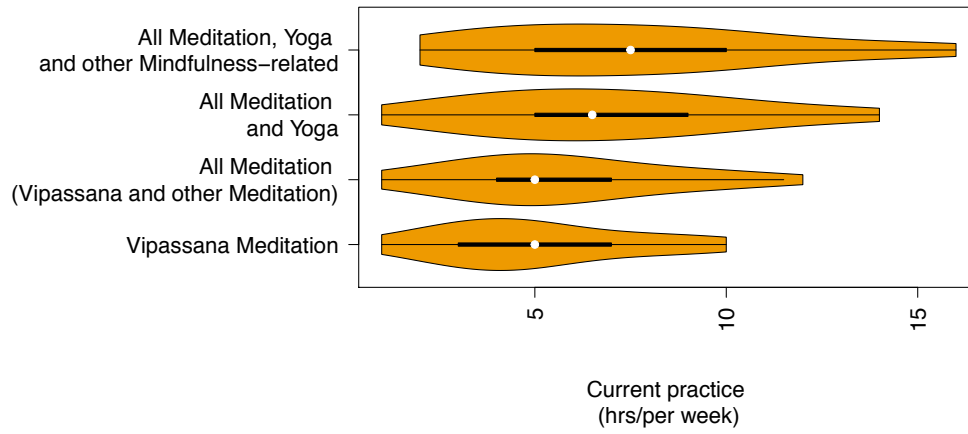


Figure A.2: Violinplot (box plot combined with kernel density plot) depicting median and distribution of current meditation and mindfulness practice. Other mindfulness-related include Qi-Gong, Tai Chi, Kung Fu.

Table A.2: Description of meditators' current meditation and mindfulness-related practice (hours/week) ($n = 22$)

Variable	M	SD	min	max
Vipassana Meditation	5.28	2.75	1	10.5
All Meditation (Vipassana, other Meditation)	5.90	2.97	1	12.0
All Meditation, Yoga	7.05	3.50	1	14.0
All Meditation, Yoga, other Mindfulness-related	7.75	3.94	2	16.0

Table A.3: Description of meditation-naïve participants' mindfulness-related experience ($n = 19$)

	<i>n</i>
No experience at all	12
No experience, indicate theoretical knowledge	1
Past experience meditation and mindfulness-related Tai Chi: 6 hrs, 5 yrs ago. Tai Chi, irregular, more than 20 years ago. Zen 8 hrs and Yoga 3 hrs, 1 year ago. Yoga experience, marginal, irregular, not at the moment.	4
Irregular current practice mindfulness-related Yoga/relaxation techniques, irregular, gives shiatsu therapy. Qi Gong, rarely, infrequent, since 1 year, self-guided.	2

Matching and group characteristics

Table A.4: Matching variables between groups

	MNP ($n = 22$)		LTM ($n = 22$)		Statistic df	p
	M	SD	M	SD		
Age	45.45	10.94	47	11.11	$t(42) = -.46$.64
Gender (f/m)	10/12		8/14		$\chi^2(1) = .094$.76
Education (years)	18.36	3.69	19.05	4.50	$t(42) = -.55$.59
IQ (MWT-B)	122.59	13.45	118.18	13.19	$t(42) = 1.10$.28

Abbreviations MWT-B Mehrfachwahl-Wortschatz-Intelligenz-Test

Table A.5: Occupation per group

Field	MNP($n = 22$)	LTM ($n = 22$)
	# working in this field	# working in this field
Retired	0	1
Student (psychology)	2	1
Business	7	5
Sciences	2	1
Humanities	2	2
Arts	1	1
Health care	2	3
Mental health care	4	6
Spiritual	1	3

Note. Groups did not differ in their general fields of occupation:

$\chi^2(8, n = 44) = 4.6, p = .79$.

Business: self-employed, employee, management, business coaches.

Sciences: ingnenieering, informatics, research.

Humanities: philosopher, teacher, translator, historian.

Health care: medical doctors, animal doctors, and caregivers outside psychiatry.

Mental health: psychologist, psychiatrist, caregivers in psychiatry, shiatsu-therapist.

Spiritual: 3 mindfulness-teachers (1 full-, 3 part-time), 1 yoga-teacher, 1 deacon.

Questionnaire results

Table A.6: Mindfulness questionnaire group results and comparisons

	MNP ($n = 22$)		LTM ($n = 22$)		Statistic (df)	p	$p(fdr)$
	M	SD	M	SD			
FFMQ							
Observe	28.00	5.91	31.45	3.38	$t(42) = -2.38$.02*	.15
Describe	30.73	6.23	32.14	3.77	$t(42) = -.91$.37	.49
Awareness	31.55	6.15	31.55	4.89	$t(42) = 0.00$	1.00	1.00
Non-judge	33.45	5.47	33.59	5.42	$t(42) = -.08$.93	1.00
Non-react	23.32	4.49	27.36	3.61	$t(42) = -3.30$.002**	.027*
SCS							
Self-kindness	3.28	1.08	3.81	1.11	$t(42) = -1.60$.12	.30
Self-judgement	2.50	1.10	2.08	.80	$t(42) = 1.44$.16	.34
Common humanity	3.05	1.03	3.28	.97	$t(42) = -.79$.43	.51
Isolation	2.03	.89	.77	.77	$t(42) = 1.36$.18	.34
Mindfulness	3.43	.89	1.69	.97	$t(42) = -.89$.38	.49
Overidentified	2.43	.95	2.11	.71	$t(42) = 1.26$.21	.35
Total	3.46	.79	3.82	.53	$t(42) = -1.77$.08	.28
TAS							
Total	39.68	10.38	35.14	6.11	$t(42) = 1.74$.09	.29

Abbreviations. FFMQ Five Facet Mindfulness Questionnaire, SCS Self-Compassion Scale

Note. A total score for the FFMQ is not usually reported.

 $p(fdr)$ corrected for 13 testsemphSignificance levels $p < .1$, $*p < .05$, $**p < .01$

Pre-/Post-scanning questionnaires

Table A.7: PANAS, tiredness and general experience during scanning

	MNP ($n = 22$)		LTM ($n = 22$)		Statistic df	p
	M	SD	M	SD		
<i>Pre-Scan</i>						
Positive affect	30.55 ^a	6.32	32.74 ^b	6.05	$t(37) = -1.10$.28
Negative affect	13.10 ^a	3.51	13.11 ^b	2.05	$t(37) = -.01$	1.00
<i>Post-Scan</i>						
Tiredness	3.95	2.01	2.86	1.61	$t(42) = 1.98$.054
Experience in scanner	6.05	1.76	6.29 ^c	1.85	$t(41) = -.44$.66
Pain	.23	.43	.38	.50 ^c	$\chi^2(1) = 0.58$.44

Abbreviations PANAS Positive and Negative Affect Schedule

Note. Tiredness and experience in the scanner were measured on a 9-point self-report Likert scale

Tiredness: 1=not at all tired, 9=very tired, Experience in the scanner: 1=very uncomfortable, 9=very comfortable

Pain was asked dichotomously: 0=no pain, 1=yes

^a $n = 20$.

^b $n = 19$.

^c $n = 21$.

Appendix B

Supplementary material study 1

Pre-/Post-scanning questionnaires

Table B.1: Task related self-report measures

	MNP ($n = 19$)		LTM ($n = 21$)		Statistic df	p
	M	SD	M	SD		
<i>Post-Scan</i>						
FEEL in	6.79 ^b	1.55	7.25 ^c	1.21	$t(37) = -1.03$.31
FEEL out	7.00	1.29 ^b	7.15	1.35 ^c	$t(37) = -0.35$.72
FEEL succ	6.47 ^b	1.61	7.10 ^c	1.55	$t(37) = -1.24$.22
FEEL verbal	5.63 ^b	1.42	6.70 ^c	1.53 ^b	$t(37) = -2.26$.030*
THINK in	7.11 ^a	1.41	7.37 ^b	1.30	$t(37) = -.58$.57
THINK out	7.11 ^a	1.57	7.16 ^b	1.38	$t(37) = -.096$.92
THINK succ	7.11	1.37	7.45	1.36 ^c	$t(37) = -.79$.43

Abbreviations succ success

Note. FEEL/THINK in/out, success, verbal measured on a 9-point discrete Likert scale

In/out: How easy was it to get *in/out* of the condition: 1=very difficult, 9=very easy.

In/out: 1=not tired, 9=very tired

Experience in the scanner: 1=very uncomfortable, 9=very comfortable.

Success: How well could you follow the instructions: 1=not at all, 9=very good.

verbal: How verbal were your experiences during FEEL.

E.g. Did you label your experiences (9=only verbal) or not (1=only perceptual).

^a $n = 18$.

^b $n = 19$.

^c $n = 20$.

Previous studies

Table B.2: Overview previous findings

Region	Study: Herwig, 2010 Sample: Naïve	Study: Farb, 2007 Sample: Naïve	Study: Farb, 2007 Sample: after MBSR
Amygdala	Amygdala/Hippocampus L	No result reported	Amygdala L
Mid-prefrontal	MPFC (and ACC) R (6) Mid anterior prefrontal (9)	No result reported Rostral MPFC (10)	No result reported Dorsal MPFC (9, 10, 32)
Other Midline	PCC (23, 31)	PCC (23, 31)	No result reported
Prefrontal lateral	DLPFC L (6/8/9) Inferior frontal L (44)	DLPFC L (46/9) Ventrolateral prefrontal L (47)	No result reported Dorsal inferolateral R (46, 45)
Somatosensory	Somatosensory cortex R (3/7/40)	No result reported	Supramarginal gyrus R (40)
Insula	Inferior frontal/Insula post R (43/6/13)	No result reported	Insula post R
Parietal	Bi-lateral	Left-sided	No result reported

Activations (red) and reduced activations (blue) during FEEL>THINK (Herwig et al., 2010) in meditation-naïve participants, and during experiential versus narrative self-reference (Farb et al., 2007) in meditation-naïve participants and participants after an MBSR course. Independent exploratory ROI analysis were conducted for regions printed in bold. Brodman areas are indicated in brackets.

ROI analysis

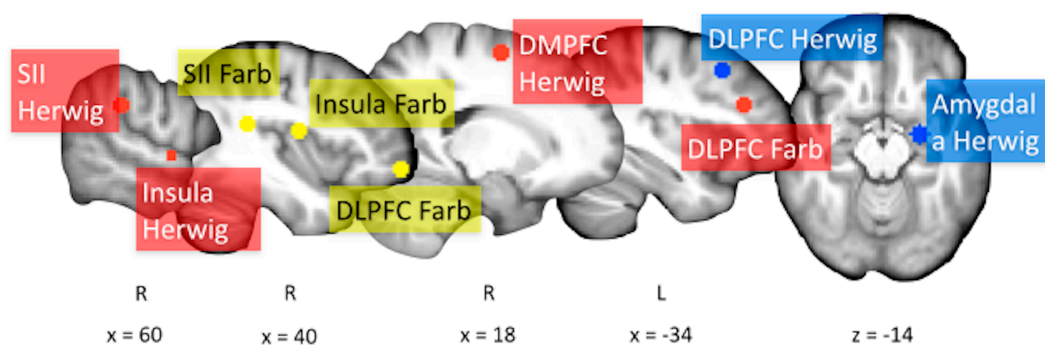


Figure B.1: Independent ROIs. Colors represent reported reduced activations (blue) and activations in meditation-naïve (red) and in mindfulness trained (yellow) participants in the studies by Herwig et al. (2010) and Farb et al. (2007). Since the amygdala overlapped between the studies, we averaged x, y, and z coordinates to create an averaged ROI. TAL to MNI conversion were obtained using the Lancaster transform implemented in GingerALE (Laird et al., 2010).

Table B.3: Independent ROI results

Region	Study	x, y, z	MNP		LTM		MNP > LTM
			Mean (SD)	t (df = 18)	Mean (SD)	t (df = 20)	t (df = 38)
Amygdala L	Avg	-25, -8, 14	-0.029(0.11)	-1.16	-0.048(0.10)	-2.29	0.58
DLPFC L	Farb	-36, 32, 24	-0.027(0.15)	-0.85	-0.028(0.15)	-0.84	-0.019
	Herwig	-32, 18, 46	0.000(0.13)	-0.02	-0.13(0.13)	-4.60	3.20
SII R	Farb	40, -40, 20	0.016(0.067)	1.03	0.0048(0.061)	0.36	0.54
	Herwig	59, -30, 30	0.26(0.034)	3.39	0.22(0.23)	4.42	0.42
Insula post R	Farb	40, -8, 16	0.011(0.13)	0.39	-0.022(0.12)	-0.84	0.85
	Herwig	55, 0, 1	0.093(0.19)	2.08	0.14(0.18)	3.64	-0.80

Abbreviations Avg average, DLPFC dorso-lateral prefrontal cortex, SII secondary somatosensory cortex, LTM mid-to-long-term meditators, MNP meditation-naive participants, R right, L left, M medial
Stereotaxic coordinates are based on the human atlas of MNI, BA are based on Talairach Daemon labels in FSL view.

Additional fMRI material

FEEL > B

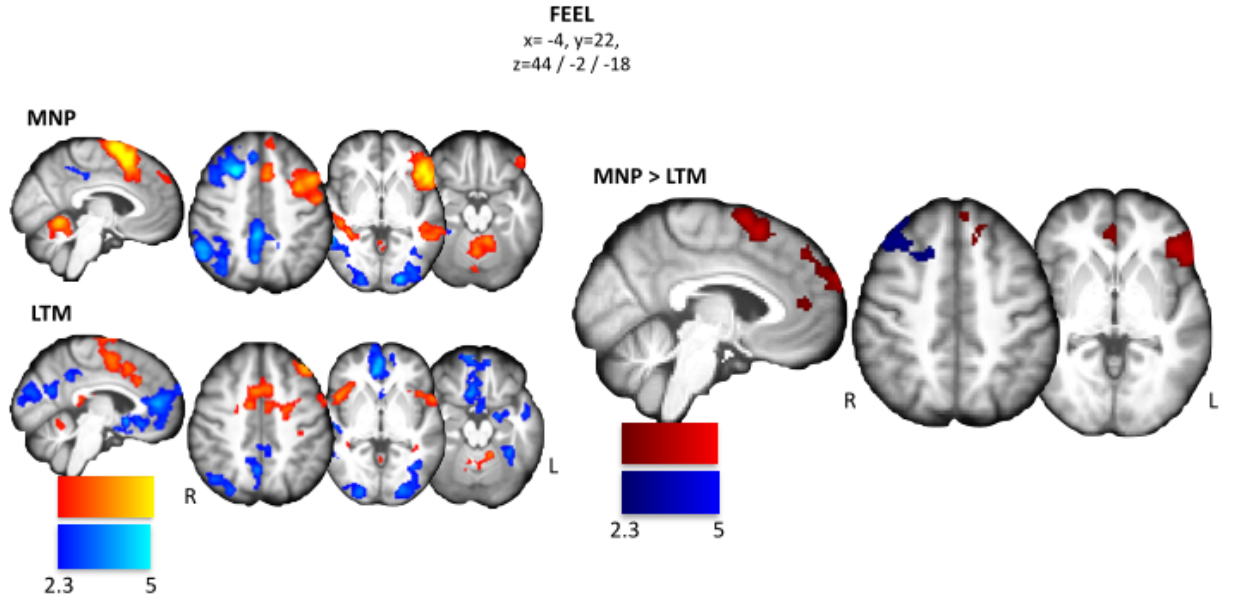


Figure B.2: Neural activations (red) and deactivations (blue) of FEEL>THINK. Probability maps depict significant results for meditators (LTM), meditation-naive participants (MNP) (light colors) and the group comparison MNP>LTM (dark colors).

Appendix C

Supplementary material study 2

Stimulus selection and evaluation

Table C.1: Individually chosen self-critical and self-praising adjectives and individual evaluation

	MNP ($n = 22$)		LTM ($n = 22$)		Statistic df	p
	M	SD	M	SD		
<i>SC</i>						
Number chosen	7.55	2.26	7.95	2.48	$t(42) = -.57$.57
Evaluation per adjective	2.81	.84	2.97	.61		
<i>NNSC</i>						
Evaluation per adjective	3.78	.56	3.67	.67		
<i>SP</i>						
Number chosen	11.36	5.32	13.18	5.57	$t(42) = -1.11$.27
Evaluation per adjective	4.30	.48	4.42	.49		

Abbreviations SC self-criticism, NNSC negative not self-critical, SP self-praise

Note. Number indicates the number of chosen adjectives from the lists of 52 positive and 52 negative adjectives

The 6 selected adjectives had to be rated on a 5 point Likert-scale

For SC “how negative do you judge these traits?”, For NNSC “how negative do you judge these traits?”

Response-scale SC and NNSC: 1=not negative, 2=slightly negative, 3=rather negative, 4=quite negative, 5=very negative

For SP “how positive do you judge these traits?”

Response-scale for SP: 1=not positive, 2=slightly positive, 3=rather positive, 4=quite positive, 5=very positive

Affective rating

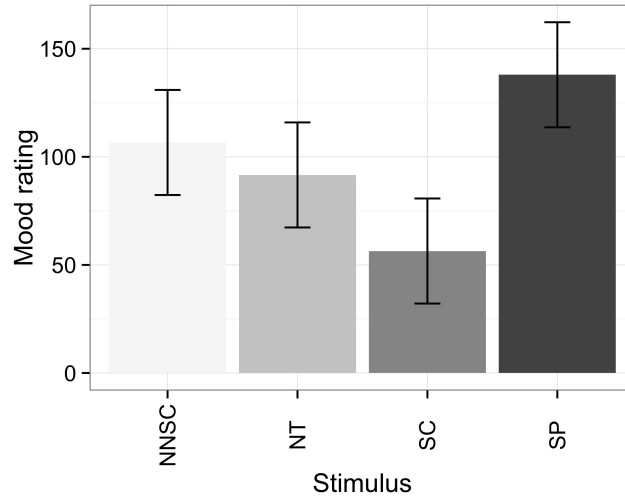


Figure C.1: The figure shows absolute mood ratings after each condition for both groups. Error bars show the 95% confidence interval. Values were first aggregated on the subject level. NNSC negative not self-critical, NT neutral, SC self-criticism, SP self-praise.

Additional fMRI results

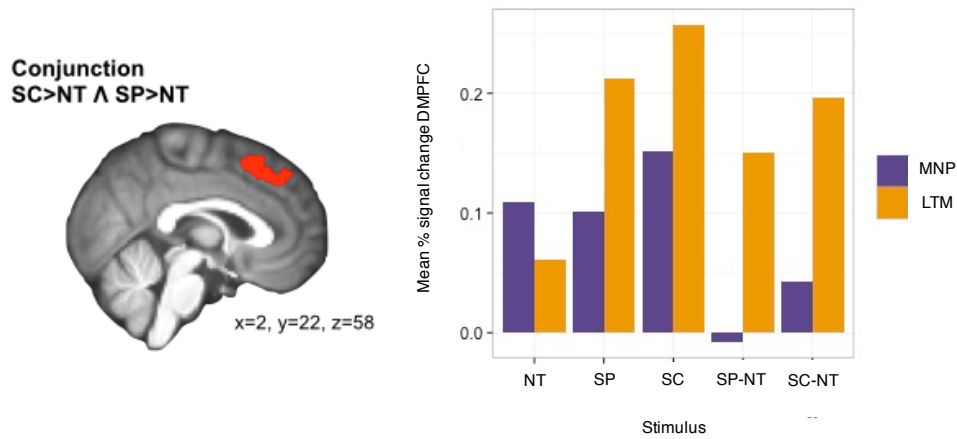


Figure C.2: Mask from the conjunction analysis, displayed on the MNI brain and mean % signal change from this region during single conditions and contrasts of interest for both groups. Statistics are not independent from mask selection. Therefore they are solely meant to illustrate the activations underlying the contrasts and group differences.

PPI schematic representation

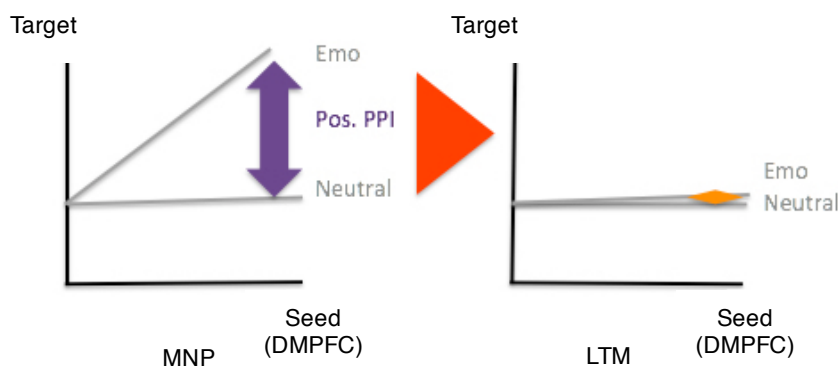


Figure C.3: Schematic representation of significant PPI effects (correlations between MPFC Seed and Target regions during Emo and Neutral conditions) in both groups (MNP and LTM) underlying the significant group difference in functional connectivity. Direct correlations between these regions were not computed, because results would not be independent and effects overestimated.

Curriculum Vitae

Jacqueline LUTZ

Date of birth March 15, 1981
Place of birth St. Gallen, Switzerland

Education

2007–2012 Master of Science in Psychology
University of Zurich

2002–2005 Bachelor of Science in Business Administration
Zurich University of Applied Sciences

1996–2001 General qualification for university entrance

Employment

2012–2015 PhD student
Psychiatric imaging, Head: Prof. Uwe Herwig
University Hospital of Psychiatry, Zurich
Supervisor: Prof. Lutz Jäncke

2012–2014 Clinical psychologist
Psychiatric day care clinic
University Hospital of Psychiatry, Zurich

2012 Statistics tutor
University of Zurich, Zurich

2010–2011 Research assistant
Project: Early recognition of psychosis
University Hospital of Psychiatry, Zurich

2010–2011 Research associate
Marketing and communications
Zurich University of Applied Sciences

Internships and visits

- | | |
|------|---|
| 2014 | Honorary Fellow
Center for investigating Healthy Minds
Head: Prof. Richard Davidson
University of Madison, Wisconsin, USA |
| 2010 | Research internship
Laboratory for clinical affective psychophysiology
Head: Prof. Cindy Yee-Bradbury
UCLA, Los Angeles, USA |

Supervised students

- | | |
|---------------|---|
| M.Sc. theses: | “Neural correlates of self-criticism and mindfulness”,
Andrea Weibel |
| B.Sc. theses: | “Reappraisal and mindfulness”, Christian Bürgi |

Publications in peer-reviewed journals

Lutz, J., Herwig, U., Opialla, S., Hittmeyer, A., Jäncke, L., Rufer, M., Grosse Holtforth, M., Brühl, A. B. (2013). Mindfulness and emotion regulation – an fMRI study. *Social Cognitive and Affective Neuroscience*, 9(6):776-785.

Opialla, S., **Lutz, J.**, Scherpiet, S., Hittmeyer, A., Jäncke, L., Rufer, M., Grosse Holtforth, M., Herwig, U., Brühl, A. B. (2015). Neural circuits of emotion regulation: a comparison of mindfulness-based and cognitive reappraisal strategies. *European Archives of Psychiatry and Clinical Neuroscience*, 265(1):45-55.

Lutz, J., Brühl, A. B., Dörig, N., Scheerer, H., Achermann, R., Weibel, A., Jäncke, L., and Herwig, U. (2016). Altered processing of self-related emotional stimuli in mindfulness meditators. *NeuroImage*, 124(Pt A):958-967.

Weidt, S., **Lutz, J.**, Rufer, M., Delsignore, A., Jakob, N. J., Herwig, U., Brühl, A. B. (in press). Common and differential alterations of general emotion processing in obsessive-compulsive and social anxiety disorder. *Psychological Medicine*.

Lutz, J., Brühl, A. B., Jäncke, L., Herwig, U. (submitted for publication). Neural correlates of mindful self-awareness in mindfulness meditators and meditation-naïve subjects revisited.